NORTH CAROLINA

Medical Journal

Vol. 15 No. 1
January, 1954

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SYMPOSIUM ON MYOCARDITIS

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1. Wilhelmj, C. M.; McDonough, J., and McCarthy, H. H.: Nutrition and Blood Pressure, Am. J. Digest. Dis. *20*:117 (May) 1953.
2. Mann, G. V., and Stare, F. J.: Nutritional Needs in Illness and Disease, J.A.M.A. *142*:409 (Feb. 11) 1950.
3. McLester, J. S., and Darby, W. J.: Nutrition and Diets in Health and Disease, ed. 6, Philadelphia, W. B. Saunders Company, 1952, pp. 519-524.
4. Levine, V. E.: The Blood Pressure of the Eskimo, Federation Proc. *1*:121 (Mar. 16) 1942.

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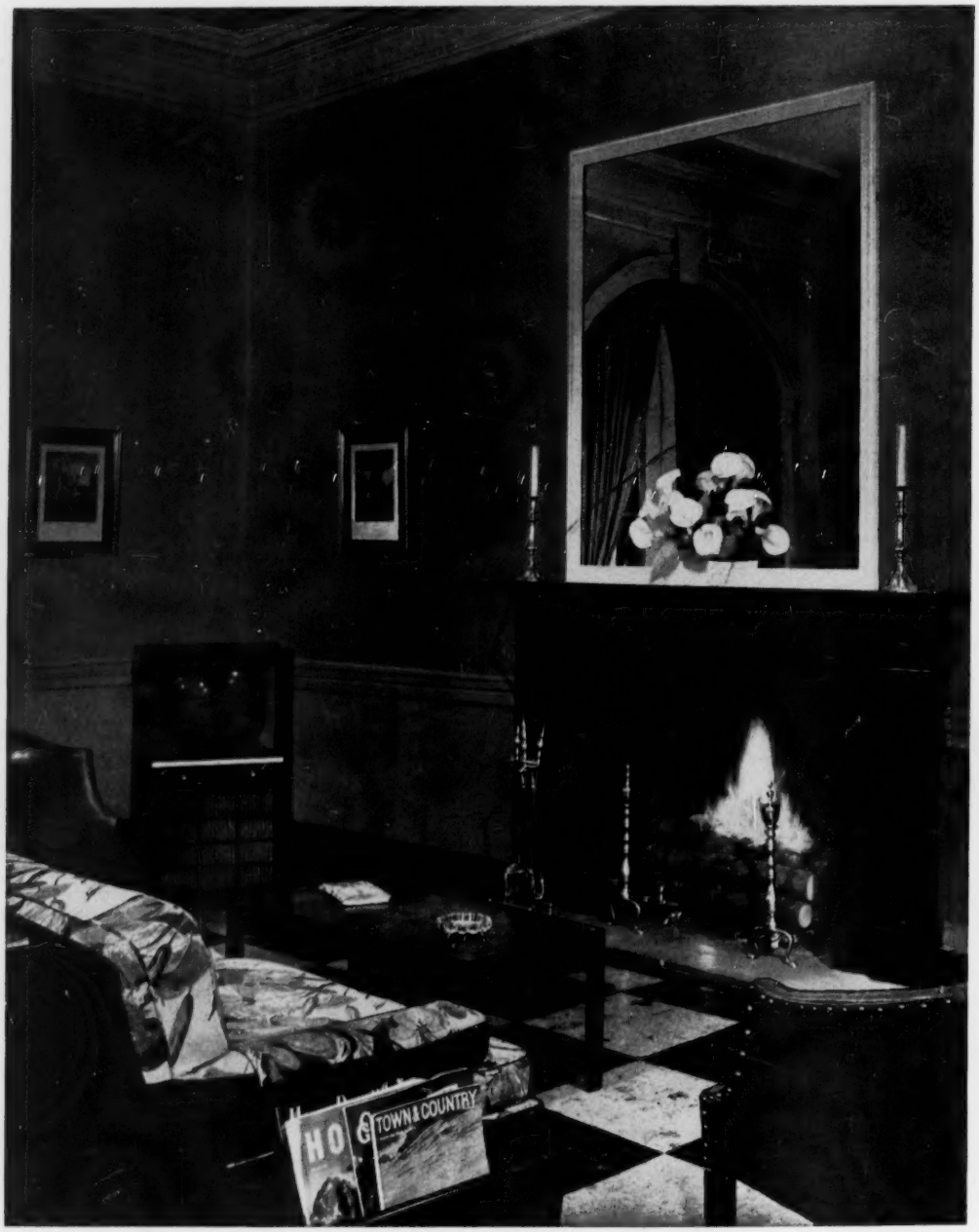

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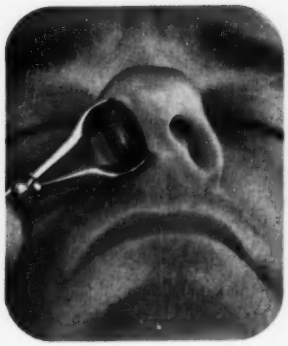

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1. Hild, A. M.: Schweiz. med. Wchnschr. 71:557, 1941.
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1. Dill, J. L.: Postgrad. Med. 4:413, 1948.

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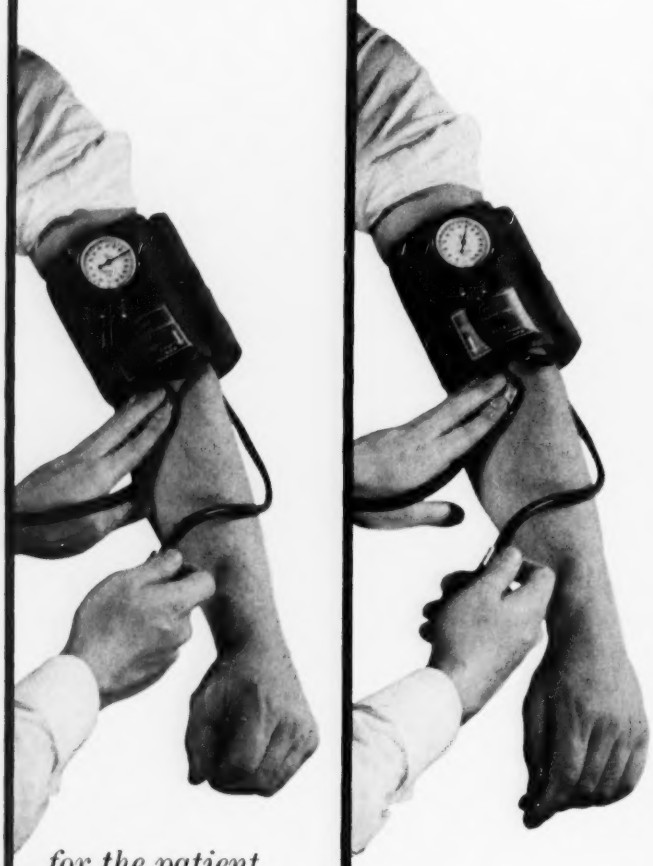

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1. Hafkenschiel, J. H., and Lindauer, M. A.: Circulation 7: 52, 1953.
2. Schroeder, H. A.: Circulation 5: 28, 1952.
3. Riven, S. S., Pocock, D. G., Kory, R. C., Roehm, D. C., Anderson R. S., and Meneely, G. R.: Am. J. Med. 14: 160, 1953.
4. Taylor, R. D., Dustan, H. P., Corcoran, A. C., and Page, I. H.: Arch. Int. Med. 90: 734, 1952.

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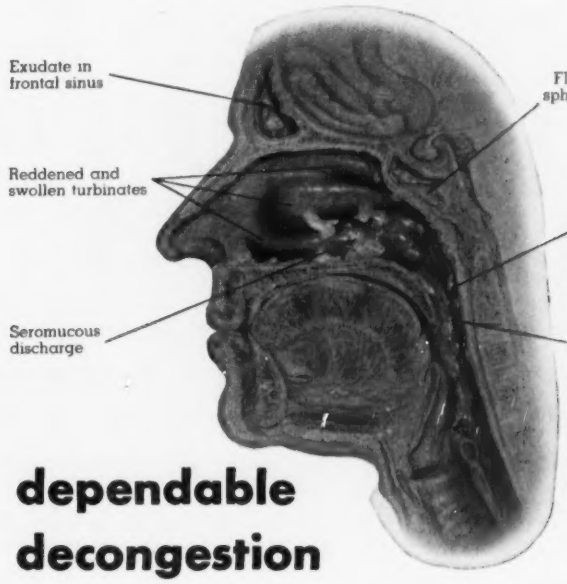

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1. Kauntze, R., and Trounce, J.: Treatment of Arterial Hypertension with Veriloid (Veratrum Viride), Lancet *2*:1002 (Dec. 1) 1951.

2. Wilkins, R. W.: Combination of Drugs in the Treatment of Essential Hypertension, Mississippi Doctor *30*:359 (Apr.) 1953.

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VOLUME 15 JANUARY, 1954 NUMBER 1

SYMPOSIUM ON MYOCARDITIS

SALIVARY GLAND VIRAL CARDITIS*

WILLIAM M. BERTON, M.D.

DURHAM

This paper concerns the histopathology of salivary gland carditis. By the choice of this terminology the cytomegalic aspect described in the literature as so typical of this infection is purposely somewhat de-emphasized. Reported cases of this viral disease appear under various names, as follows: "protozoan-like cells" as found in scattered organs of infants, "inclusion disease," "cytomegalic inclusion disease," "inclusion disease of infancy," and "salivary gland virus inclusion disease."

Historical Review

The cytopathology typical of this infection was first noted in the year 1881 by Ribbert[1], who found the parasitized cells in the kidneys of a stillborn luetic infant. It was not until 1904, however, that Jesionek and Kiolemenglou[2] described this lesion as a separate entity, involving, in their particular case, the kidneys, lungs, and liver of another syphilitic infant. These authors first interpreted the enlarged inclusion-containing cells as being protozoan in nature. In 1907 Lowenstein found similar cells in a series of 4 infants, ranging in age from 2 to 10 months.

Throughout this earlier literature the parasitized cell was generally thought to be a protozoan. Thus, in 1914 Smith and Weidman termed this so-called organism *"Endameba mortinatalium."* In 1921 Goodpasture and Talbot[3], on reviewing the reported cases and studying a case of their own, interpreted the remarkable cellular changes as a new type of abnormal cytomorphosis resulting from the action of an unknown etiologic agent. These authors were the first to recognize the inclusion bodies as such and to point out their resemblance to those inclusions formed in cutaneous lesions caused by the varicella virus, as described by Tyzzer in 1906. They also noted the peculiar changes present in ductal epithelial cells of guinea pig salivary glands, concluding that this cellular transformation was similar to that occurring in the tissues of infants.

The first reported case of typical lesions occurring in the adult was published in 1925 by von Glahn and Pappenheimer, who also identified these lesions with parasitization by an unknown virus. More historical cases, numerous case reports, statistical reviews, and reports of small series of cases of this infection in both infants and adults have since appeared in the literature. For recent, more detailed analysis of the various clinical manifestations, the associated conditions, the host parasite relationships, and histopathologic lesions reference should be made to the papers of Smith and Vellios[4], Cappell and McFarlane[5], Worth and Howard[6], and still more recently the reviews of Kidder[7] and Wyatt and others[8].

Etiology

In 1920 Jackson[9] called attention to peculiar large cells in the salivary gland ductal epithelium of guinea pigs, interpreting the inclusion bodies as a form of intracellular protozoan, most likely in a vegetative form, the sexual cycle occurring in another site. The viral etiology of these inclusions was not successfully demonstrated until 1926, when Cole and Kuttner[10] isolated a filterable virus from the submaxillary gland of infected guinea pigs. This virus has been successfully passed through short series of these animals, producing experimental lesions not only in the submaxillary salivary glands but also in other organs. Multiple investigative techniques have added to the knowledge of the virus responsible for ani-

Presented before the Section on Pathology, Medical Society of the State of North Carolina, Pinehurst, May 13, 1953.

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mal infection, and in the majority of instances there has been a significant correlation between the experimental observations and those made on human material. Multiple histochemical techniques have been profitably applied in the study of the involved tissues of both animals and human beings[5,8,11]. To date, all studies indicate that the typical inclusions are of viral origin rather than a product of toxic or degenerative cellular processes. This is of special importance, because the diagnosis is completely dependent on the presence of the typical inclusion-bearing cells. This virus is thought to be, as stated, species specific, and thus the human strain cannot be transmitted to the experimental animal. Controlled experiments designed to demonstrate diagnostically significant serologic changes in the infected animal have proven inconclusive.

The following case, previously reported by Worth and Howard[16] and presented here for further consideration, is the only reported instance in which the myocardium has been parasitized by this virus. Since, to our knowledge, the cardiac lesions have never been described in experimental animals, it is regarded as of special significance.

Review of Case

A 6 week old white male was admitted to Duke Hospital from Asheville, North Carolina, one day before death, with the chief complaint of diarrhea and an enlarged spleen. This patient was the second, full term, spontaneously delivered child of a 20 year old, type O, Rh positive, healthy woman. The infant had had transient jaundice at birth, which disappeared within five days. The mother and child were discharged from the hospital in good health. The patient was readmitted on the tenth day of life because of severe hemorrhage from the stump of the umbilical cord. He was treated primarily with transfusions of blood from the father. At the age of 3 weeks the patient had the onset of diarrheal stools numbering 10 to 12 per day, all described as malodorous and of greenish brown color. The mother reported that on two occasions blood was noted in the stool. No other signs or symptoms referable to the gastrointestinal tract were observed. A local physician at this time observed, in addition to the patient's poor general condition, an enlargement of the spleen. The child was given medication and various formulas, and was removed from breast feedings. Despite treatment, he failed to improve and progressively lost weight. He was referred to Duke Hospital for consultation and further therapy. The history otherwise is essentially noncontributory. During this period the patient's 3 year old sibling had no illnesses and was in good health.

Physical examination

On entry the physical examination revealed a moderately dehydrated, poorly nourished white male infant with a temperature of 38.2 C. (100.8 F.), a respiratory rate of 30 per minute, and a rapid, regular pulse. Excoriation of the skin of the buttocks and scrotum as well as a macular rash over the head and forehead was noted. There was a small cutaneous abscess behind the right ear. Both the liver and spleen were palpable, the spleen being the more remarkably enlarged. Otherwise, no remarkable lesions were noted.

Accessory clinical findings

The accessory clinical examinations revealed a red blood count of 3,500,000, a hemoglobin content of 9.5 Gm., a white blood cell count of 13,500, with a differential count of 28 per cent segmented forms, 34 per cent stab forms, 7 per cent juvenile forms, 18 per cent large lymphocytes, 10 per cent small lymphocytes, and 3 per cent monocytes. The urine was negative, and the stools were formed, greenish brown, and negative for parasites, ova, mucus, pus, and blood. Stool cultures for pathogens were negative, as were the Kahn, Kline, Wassermann and Mazzini tests for syphilis. On entry a carbon dioxide combining power of 21.7 volumes per 100 cc. was noted.

Course in hospital

On the day of admission 60 cc. of 1/6 molar lactate solution was given in an attempt to overcome the patient's dehydration. A corresponding rise in the carbon dioxide combining power was noted. During the night three formed yellow stools were passed. Despite the further administration of fluids by clysis and by mouth, the patient did poorly, becoming progressively weaker, and expired quietly in the evening of the second hospital day. The final clinical impression was that of dehydration secondary to diarrhea of the newborn and splenomegaly of undetermined etiology, most likely infectious.

Postmortem examination

The body was that of a 2,580 Gm. white male child measuring 49 cm. from crown to heel and 31 cm. from crown to rump. A generalized icterus, a raised, purple-red ulcerative lesion behind the right ear, pin-point petechiae over the hands, feet and trunk, and excoriations of the skin of the buttocks and scrotum were noted on external examination. Scattered small hemorrhages were seen bilaterally in the muscles of the flanks. The spleen and liver were both enlarged, the spleen weighing 42 Gm., the liver 180 Gm. The spleen was wrinkled and firm, with, on cut surface, indistinct malpighian bodies. The liver was grossly remarkable only because focal areas appeared to contain increased bile pigment. The lungs and heart showed no grossly discernible lesions, even though both pleural cavities and the pericardial cavity each contained 3 to 4 cc. of clear fluid. The visceral surfaces of the lungs and heart were smooth. The heart showed a patent ductus arteriosus and foramen ovale. Petechial hemorrhages were seen in focal areas of the gastrointestinal tract, bladder, and testicles. There was generalized hyperplasia of lymphoid tissue, including the Peyer's patches. Otherwise, the viscera appeared normal. The brain showed a single focus of hemorrhage involving caudate nucleus and surface of the thalamus on the right. Cultures obtained at autopsy revealed a hemolytic and nonhemolytic *Staphylococcus albus* in the left lung. Since the nature of this disease was not grossly apparent, no viral studies were instituted.

No attempt will be made to discuss the many microscopic lesions found in the tissues of this infant. It is sufficient to note that inclusion-bearing cells resembling those of inclusion body disease of the salivary gland viral type were demonstrated in the brain, bone marrow, sweat glands, pituitary body, lungs, liver, kidney, pancreas, thyroid, various endothelial cells, intestines, spleen, adrenal glands, epididymis, testis, and heart. For detailed descriptions of the various lesions in the organs other than the heart, see Worth and Howard[6]. Our interest here relates to the myocardial lesion.

Microscopic examination of the heart

Since the histologic character of the cardiac lesions was not emphasized in the original report of this case, and since this is the only instance of cardiac parasitization recorded in the literature, it was decided that this lesion should be re-emphasized and more meticulously described.

Under the scanning lens the myocardium showed scattered focal lesions characterized by progressive replacement of extensively altered muscle fibers by a loose, fibrillar to relatively compact connective tissue. A moderate to minimal cellular infiltrate with a degree of edema was also present. Tinctorial changes accompanied by loss of cross striations and occasional moderate increases in width of certain of the myocardial fibers could be seen. In those fibers containing the typical intranuclear inclusions, a relative increase in size and peculiar "bird's eye" or "owl's eye" configuration of the nuclear structure was a constant feature.

At a somewhat higher magnification (fig. 1) the parasitized myocardial fibers showed plainly not only the absent to moderate cytomegaly, but also remarkable changes in their internal structure and protoplasmic staining properties. The alterations of the protoplasm as seen in hematoxylin-eosin preparations of Zenker formal-fixed material consisted of loss of the usual eosinophilia with relative basophilia, clumping of the sarcoplasm, and fragmenting of the myofibrillae, resulting in loss of cross striations. The intranuclear inclusion was well demonstrated under high power, the nucleus showing the characteristic configuration. The affected fibers were usually peripheral to the central fibrous portion of the lesion.

The infiltrate consisted predominantly of large mononuclear cells of probable reticuloendothelial origin, and of small round cells of the plasma cell and lymphoid type. These elements were diffusely scattered within the affected area. Polymorphonuclear leukocytes could be observed here and there. In addition to the inflammatory cells, there was an increase of fibroblasts, these cells appearing to be in different stages of maturation. The small vascular channels of the involved region showed no remarkable proliferation, although they did appear prominent, interpreted as secondary to degeneration of muscle fibers.

With still higher magnification (fig. 2) the changes associated with the intranuclear inclusions become clearly visible. The inclusion body was eosinophilic, in contrast to the surrounding basophilic chromatin material. It was homogeneous, sharply defined, and

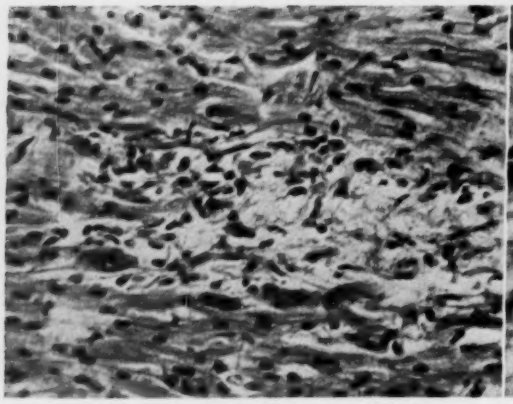

Fig. 1. Photomicrograph of myocardial lesion showing the cellular response and fibrosis. (X 383.)

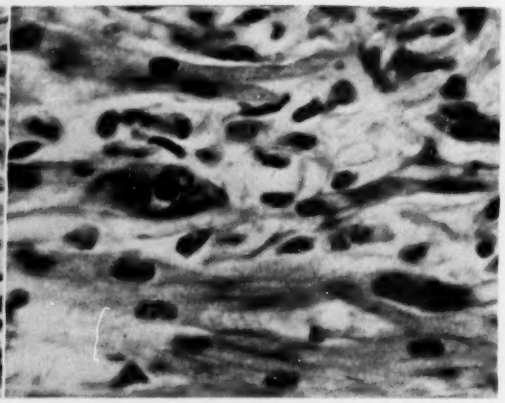

Fig. 2. Photomicrograph showing the typical intranuclear inclusion bodies. (X 871.)

centrally situated within the nuclear membrane. Surrounding the inclusion was a clear halo at the periphery, of which and just inside the nuclear membrane could be seen fine granules of densely basophilic chromatin. The nuclei of involved fibers sometimes exhibited no sharply defined inclusion, but instead simply showed hyperchromatic staining properties and an abnormal distribution of chromatin.

Again with high magnification, a few well defined eosinophilic inclusions, each surrounded by a halo, could be seen within the granular sarcoplasm of infected muscle fibers (fig. 3 and 4). These bodies, in contrast to the granular appearance of the sarcoplasm, appeared homogeneous and, in contrast to the intracytoplasmic inclusions generally described in this infection, showed little evidence of basophilia. On occasion they were observed to indent a nearby nucleus (fig. 4). Somewhat similar acidophilic inclusions were found in other cells in this case and are more fully described by Worth and Howard.

Smaller irregular basophilic granules were occasionally seen within the altered sarcoplasm. These structures may represent inclusion forms similar to those basophilic intracytoplasmic inclusions described by Pearson[12] and Farber and Wolbach[13] as characteristic of salivary gland virus disease. In this case and in this particular site, however, the larger acidophilic inclusions are most remarkable. The destruction and clumping of the myofibrils, with subsequent loss of cross-striation, is strikingly apparent. It is significant that, even with the formation of cytoplasmic inclusions, the size of the parasitized cells was not impressively in-

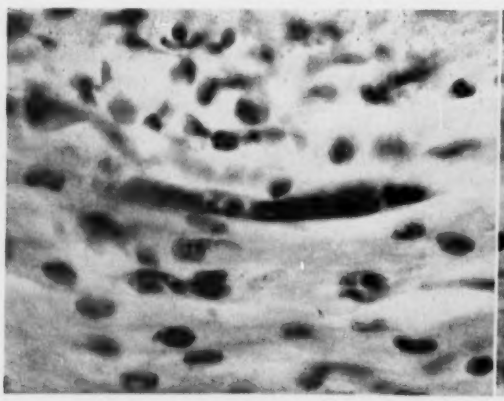

Fig. 3. Photomicrograph showing sarcoplasmic alterations and formation of intrasarcoplasmic inclusion within a myocardial fiber. (X 871.)

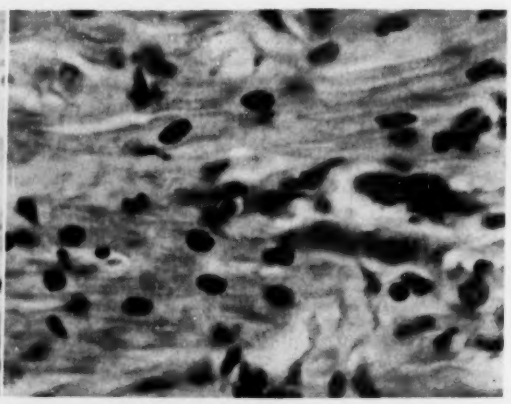

Fig. 4. Photomicrograph showing indentation of nucleus by intrasarcoplasmic inclusions. (X 871.)

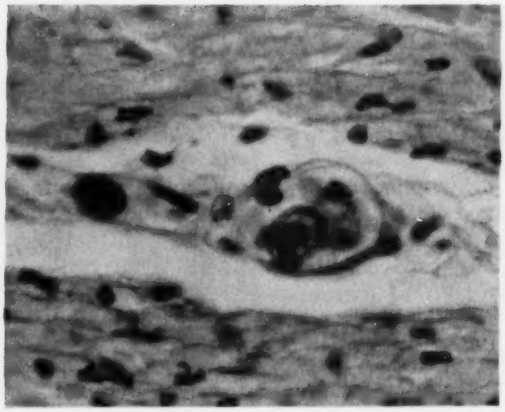

Fig. 5. Photomicrograph showing inclusion-bearing endothelial cells. (X 957.)

creased. Characteristically, muscle fibers and their nuclei are invaded by this virus as just described. At the same time, however, endothelial cells, especially those of small vessels, become parasitized (fig. 5). In these cells the cytomegaly is striking. With parasitization of the endothelium, it would not have been surprising to find small vascular channels functionally occluded, but evidence of this was not observed. In all the remaining affected tissues, with the exception of the heart muscle fibers, as noted, the parasitized cells presented conspicuous cytomegaly. This is well illustrated in the several photomicrographs in the previously cited paper by Worth and Howard.

Summary and Conclusions

This is the first and only reported case of inclusion disease in which striated muscle, particularly heart muscle, is affected. It is suggested, therefore, that we may be dealing with an infection of unusually high virulence by a variant of the salivary gland virus. Rosenbusch and Lucas[14] appear to have shown in their studies of this disease in guinea pigs that variations in virulence may be genuine.

Associated with invasion of the muscle fibers is minimal inflammatory exudate composed principally of round cells. This inflammatory reaction occurs also in other tissues than the myocardium, and is well known in the literature. Occasionally the cellular reaction may attain massive proportions and dominate the histologic picture. In some of the reported cases epithelioid and giant cells of the foreign body type appear in the exudate.

In the myocardium typical cytomegaly occurs when endothelial cells are infected, but this is inconspicuous when the muscle fiber is parasitized. In the muscle fibers the prominent structural changes consist of the formation of intranuclear and intrasarcoplastic inclusions, fragmentation of the myofibrils, and loss of the usual cross striation.

The diagnosis of salivary gland virus inclusion disease is entirely dependent upon the finding of lesions in which the typical viral inclusions are demonstrable. This is emphasized by Pinkerton[11a] in a recent paper wherein he discusses the inclusions formed by a variety of viral infections. The identification of the etiologic agent producing the lesions as seen in the heart muscle described in this paper was accomplished solely on the finding of the described inclusion-bearing cells. The other characteristics of the myocardial lesions are considered to be secondary to degeneration of the parasitized muscle fiber and to the healing by fibrosis which follows.

Since submission of this paper for publication, two articles in which myocarditis in cases of generalized salivary gland viral infections is described have appeared in the literature. These references are as follows: (a) Ahvenainen, E. K.: Inclusion Disease or Generalized Salivary Gland Virus Infection. Report of Five Cases, Acta Pathologica et Microbiologica Scandinavica Supplementum 93:159-167, 1952. (b) Bacala, J. C., and Burke, R. J.: Generalized Cytomegalic Inclusion Disease, Journal of Pediatrics, 43:712-719 (Dec.) 1953.

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ISOLATED MYOCARDITIS IN INFANTS AND CHILDREN*

Report of Five Cases

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By definition, isolated myocarditis is an inflammatory and degenerative process of the myocardium occurring without endocarditis or pericarditis, and without relation to infection in other organs or those agents known to produce myocarditis.

The condition has been termed interstitial myocarditis, myocarditis perniciosa, diffuse granulomatous myocarditis, and idiopathic, productive, and eosinophilic myocarditis. It often bears the name "Fiedler's myocarditis." Fiedler[1] applied the term "interstitial" in his description of the process, but Schmorl is said to have noted parenchymatous degeneration as well as the interstitial inflammatory exudate in Fiedler's cases. The term "isolated" was first used by Sellentin[2] to indicate the absence of other significant disease processes in the patients whom he described.

Interest in this country was stimulated in 1929 by Scott and Saphir[3], who reported 2 cases. Since that time, and particularly since the appearance of Saphir's extensive review of myocarditis in 1942[4], an increasing interest in cases of this type has been evident, with reports of an increasing spectrum of agents thought to be of etiologic significance.

Two types of the disease are described—the more frequent, a diffuse inflammatory reaction characterized by the presence of mononuclear phagocytes, eosinophilic and neutrophilic granulocytes, and lymphocytes in varying quantitative relationships. Usually degenerative changes are found in the myocardium. Occasionally muscle giant cells are found in this form, as well as in the more unusual second type, known as "granulomatous myocarditis."[5]

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Etiology

A summary of the etiologic factors which have been under investigation illustrates the wide variety of agents involved in the problem of myocarditis in general.

Infections

Diphtheria: Gore[6], Solomon and Irwin[7], Greene[8], and others have recently described the clinical and pathologic lesions of the heart in instances of diphtheria. The toxin of this organism has been known for many years to produce myocardial injury.

Pneumonia: The occurrence of myocarditis in association with pneumonia of various types also has been known for many years. Saphir and Amromin[9] noted histologic alterations in 26 of 67 patients dying of pneumonia. Pneumonia developed in the 4 children reported by House[10], probably late in the course of myocarditis.

Syphilis has long been incriminated as an etiologic agent, but the nature and even the existence of syphilitic myocarditis are controversial. Nevertheless, there have been recorded in recent years a few cases in which syphilis had to be considered as a serious etiologic possibility, although no organisms were found in the myocardium[11].

Rickettsial: In patients dying of Rocky Mountain Spotted Fever, myocardial lesions are regularly encountered and have been adequately described by Lillie[12]. Typhus, scrub typhus, tsutsugamushi fever, and virtually every other rickettsial infection known is associated with vascular lesions, often occurring in the heart in varying degrees of severity.

Viral: The literature on this subject has been summarized by Saphir[13]. A few agents have been isolated from the tissues, while others have been seen in association with known infections and incriminated as etiologic agents in myocarditis on circumstantial evidence. Helwig and Schmidt[14] isolated a virus from the heart of an anthropoid ape which died suddenly, and were able to reproduce myocarditis in guinea pigs, and myocarditis and encephalitis in mice and hamsters. The lesions resembled those of human myocarditis. Among Army personnel in the

Philippines, 17 patients with a "three day fever" were found to have neutralizing antibodies to this virus[15], which has been termed "virus of encephalomyocarditis," of which several closely related strains have been described. Influenza, type A, has been isolated from the lung of a patient with severe myocarditis, in whom relatively little disease was found in the lung itself[16]. The occurrence of myocarditis in poliomyelitis has been noted by Ludden and Edwards[17] in 40 per cent of their cases and by Saphir and Wile[18], Dolgopol and Cragan[19], and others. The list of other virus infections associated with myocarditis includes infectious mononucleosis, epidemic hepatitis, yellow fever, smallpox, dengue, atypical pneumonia, measles, mumps[20], Rubella, influenzal-like infections, and epidemic encephalitis[21].

Streptococci: Schenken and Coleman[22], and Schenken and Heibner[23] have described 2 cases in which a micro-aerophilic streptococcus was cultured from the heart at autopsy in cases otherwise diagnosed as "isolated myocarditis." They considered the organism significant etiologically. Roulet[24] described a case in which streptococcic septicemia was associated with a diffuse myocarditis. Mallory and Keefer[25] described endocardial and myocardial proliferative and degenerative changes in patients dying of streptococcic infections.

Meningococci, typhoid, pseudomonas, and a wide variety of *other organisms* produce lesions of the heart, usually focal and in association with obvious disease in other organs.

The *miscellaneous infections* have included nasopharyngitis and tonsillitis, of which Gore and Saphir[26] described 35 cases. It is of interest that streptococci were isolated in 15 of their patients, either clinically or at autopsy. A striking correlation between myocardial injury and recurrence of upper respiratory infection due to streptococci has been shown by Rantz, Boisvert and Spink[27] in regard to rheumatic fever with carditis. Myocarditis has been reported in association with acute and subacute glomerulonephritis, by Gore and Saphir[28] who found the myocardium involved in 10 per cent of 160 cases. In nephritis the lesion was characteristically serous as opposed to the more cellular reaction associated with nasopharyngitis. Other instances of myocardial involvement have been found in toxoplasmosis, sarcosporidiosis, histoplasmosis, tuberculosis, and a multitude of other infections.

Hypersensitivity

The factors of hypersensitivity have also been brought under investigation. Jaffe[29] found 500 cases of myocarditis in 5,000 autopsies in Venezuela, the majority being associated with other diseases such as syphilis (44 per cent), bilharziasis (48 per cent), and necatoriasis (28 per cent). These diseases were found much more frequently in the cases of myocarditis than in the general series. He considered hypersensitivity to be a factor in the development of myocarditis. Later, working with Holz[30], he produced lesions in the myocardium similar to those found in human beings, by the injection of heart extract, serum and egg albumin, alone or in combination. The use of heart extract in combination with one or the other of these substances is said to have produced the more severe lesions.

Using the methods of Rich and Gregory[31], Kyser[32] produced myocarditis, and found that he could prevent the formation of the lesions by the use of antihistaminic drugs administered throughout the experiments.

Hypersensitivity to the sulfonamides has been recognized since the paper of French and Weller[33] as a probable factor in the etiology of myocarditis, and its widespread use necessarily brings it under suspicion in any case in which other factors can be eliminated. Serum disease has also been discussed as a causative factor[34].

Metabolic and dietary factors

Dietary factors have been implicated etiologically by Smith and Furth[35] and by Toreson[36] in patients who were on a deficient diet over long periods of time, and in whom severe inflammatory and degenerative changes of the myocardium developed. They considered that their cases were probably instances of beri-beri heart disease, in accord with the work of Wenckeback[37] and of Weiss and Wilkins[38]. Foci of necrosis have been found in the hearts of vitamin E deficient rabbits by Bragdon and Levine[39].

Hypokaliemia has been implicated by Rodriguez, Wolfe and Bergstrom[40]. Aberrations of the electrocardiogram are well known in patients deficient in potassium, but the focal myocardial inflammatory and degenerative lesions are seldom encountered.

Follis and his colleagues[41] have produced changes in the hearts of experimental animals by a diet deficient in potassium and high in protein. A period of eight days was required for their development.

Other factors

Among other factors thought to produce myocarditis are pregnancy[42], burns, hypothyroidism, status thymicolymphaticus[43], and toxic chemical agents such as arsenic[44] and carbon monoxide.

Cases of Undetermined Etiology

There are many instances of myocarditis reported in which no specific etiologic agent can be found even with the foregoing factors in mind. It is this group in which we are particularly interested. In comparison to adults, relatively few cases of myocarditis of this "isolated type" have been reported in children. Tedeschi and Stevenson[45] found 35 cases in the literature up to 1944. Numerous others have been reported since[45,46].

This group of poorly understood cases seem to develop spontaneously or in association with some other mild disease process, most often nasopharyngitis. The symptoms and signs are usually mild until late in the disease when tachycardia, hypotension, cyanosis, and cardiac enlargement, sometimes of such degree as to suggest pericardial effusion, develop. Chest pain is occasionally a complaint. The course is rapid, sometimes terminating in hours and occasionally extending as long as three weeks or more. Death is commonly unexpected, and more often than not it is sudden.

The findings at autopsy consist usually of a large, pale flabby heart, more tan than red, with little or no epicardial or endocardial change. The enlargement is due to dilatation and to inflammatory changes in the myocardium. Evidence of congestive failure is frequently found, and there may be associated pneumonia of varying degrees, enlargement of mesenteric and mediastinal lymph nodes, and hyperplasia of the spleen. The microscopic lesions vary from a mild to prominent serous exudate with scattered histiocytes and no evident destruction of the parenchyma to severe necrosis of myocardial fibers with a dense exudate of lymphocytes, histiocytes and granulocytes and, occasionally, many multinucleated giant cells, derived from muscle cells and wandering histiocytes. The usual lesion lies between these extremes, with edema, fragmentation of the fibers, and an inflammatory exudate of lymphocytes, histiocytes and neutrophils in varying proportions occurring either focally or diffusely. Eosinophils are numerous in some cases and absent in others. Scarring appears late in the more protracted cases, but usually the short course of the disease does not allow time for its development.

The clinical course and autopsy findings are much the same in children as in adults. In reviewing the files of The Bowman Gray School of Medicine, 3 cases which met the criteria were found in a total of approximately 2500 autopsies. Dr. Wiley D. Forbus has been kind enough to allow me to report two cases which have been studied in the Department of Pathology of Duke University.

Reports of Cases

Case 1

A 7 months' old white male infant was born at term by normal delivery. He had been well until suddenly on the day of admission he became cyanotic and had difficulty in breathing. Tachycardia of unknown degree was present, and the heart was thought to be enlarged to the right. Accentuated hilar shadows were found on roentgen examination and interpreted as pneumonia. The white blood cell count was 13,000, the hemoglobin 6.5 Gm., and platelet count 250,000. There was poor response to antibiotics, and the child died unexpectedly on the third day of illness. The temperature had never been particularly elevated until the day of death, when it rose to 102 F.

At autopsy (performed in an outside hospital) the pericardial sac contained about 15 cc. of straw-colored fluid. The heart appeared enlarged and weighed 70 Gm. (normal, 34 Gm.). No endocardial or epicardial lesions were noted grossly. The myocardium was brownish-red in color. Both ventricles were dilated and flabby. The lungs were heavy and peripherally aerated, with a wide zone of hyperemia and apparent consolidation in the hilar regions.

The spleen weighed 40 Gm. (normal 20 Gm.). The malpighian bodies were unusually prominent. No changes were noted in the gastrointestinal tract or adrenal glands, but the kidneys were hyperemic.

On microscopic examination, all areas of the myocardium were infiltrated diffusely, with focal accentuations, by lymphocytes and histiocytes. Neutrophilic leukocytes and eosinophils could not be found. In the areas of focal accentuation particularly, the myocardial fibers were fragmented, and the infiltrate appeared within the fibers. Otherwise diffuse changes consisting of loss of striation, granular degeneration, and nuclear pyknosis occurred. No specific vascular disease was noted, other than a few small agonal thrombi in the small veins. The epicardium and endocardium were free of lesions except for an occasional extension of the inflammatory reaction into the deep layer of the epicardium, and some proliferation of endothelial lining cells. The inflammatory reaction was more intense in the outer one third of the myocardium. Atrial involvement was similar to that of the ventricles.

In the lungs edema was intense, with numerous lymphocytes, macrophages, and an occasional neutrophilic and eosinophilic granulocyte in the alveoli.

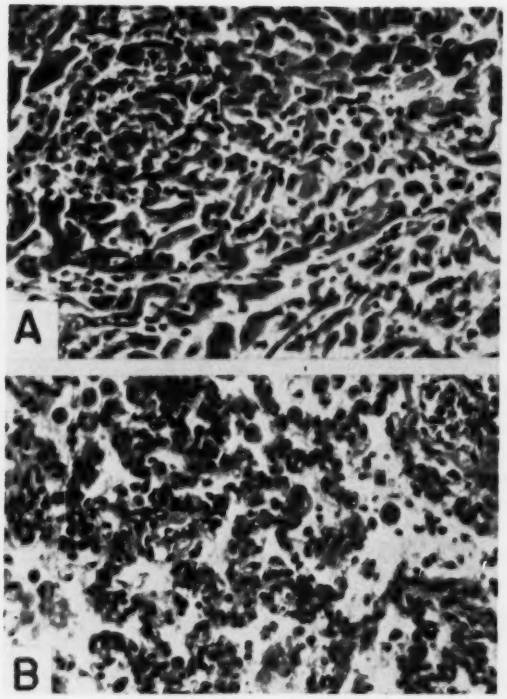

Fig. 1. (Case 1) A. The myocardial inflammatory reaction, interstitial edema and degeneration of the muscle fibers are shown here. B. Pulmonary hyperemia, edema, and the numerous phagocytes in the alveolar spaces.

The interstitial spaces contained exudate of the same type. No organisms could be found in sections of the heart and lungs stained by MacCollum's method for bacteria.

In the liver, edema was prominent in the spaces of Disse. Many of the hepatic cells were swollen, and contained droplets of sudanophilic material. Hyperemia of the spleen and hyperplasia of the germinal follicles were prominent. Virtually every follicle showed necrosis at the center.

In the kidneys, the pelves were normal. Evidence of glomerular injury could be found in every area examined. Endothelial proliferation without obstruction was present, with areas of hyaline thickening of the capillary walls, and occasional neutrophilic granulocytes in these areas. No hyaline change or other lesion of the vessels was found. There was occasionally some proliferation of the lining cells of Bowman's capsule. The tubules showed no injury.

Case 2

This 18 month old white female was admitted to an outside hospital with a history of fever, headaches, cold, and vomiting of unknown duration. The temperature was 102.6 F. A vague history of "asthma" was obtained. The child was restless and vomited on several occasions. Treatment with Terramycin, Emetrol and Luminal was without avail, and she died approximately three hours after admission.

At autopsy done in the outside hospital the body was found to be well developed and well nourished, with frothy sanguineous mucus exuding from the mouth and nose. Cyanosis was not noted. Approxi-

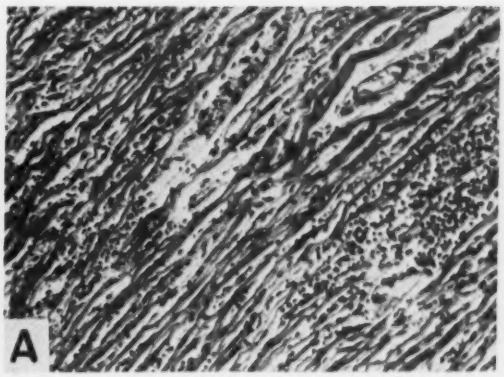

Fig. 2. (Case 2). The myocardial inflammatory reaction.

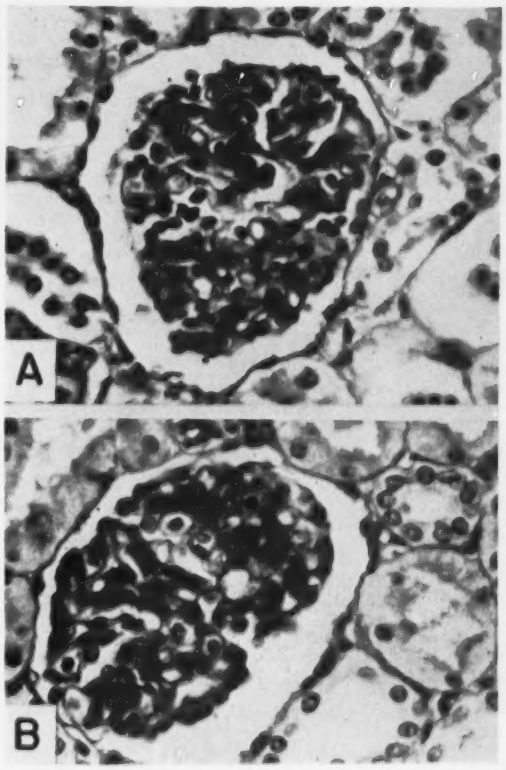

Fig. 3. A (Case 1). B (Case 2). Thickening and fuzziness of the capillary basement membranes, with some endothelial proliferation are shown here. The change is not so striking in this photograph as in the sections.

mately 200 cc. of clear serous fluid was present in the right pleural cavity, and about 15 cc. each in the left pleural and peritoneal cavities. The heart was enlarged, but could not be weighed. The right ventricle in particular was dilated. No endocardial or epicardial lesions were found. In the lungs all

five lobes were rather firm and rubbery, with mottled purple areas on the cut surface. The liver extended 3 cm. below the costal margin, and was mottled grayish-tan. No lesions were noted in the biliary system. The intestinal tract was clear. In the spleen some enlargement was noted grossly, and malpighian bodies were unusually prominent. Lymph nodes of the mesentery and mediastinum were enlarged, soft, and rubbery. The kidneys showed no gross lesions. The brain was not examined.

Microscopically, there was a diffuse edema, with interstitial foci of lymphocytes and an occasional plasma cell and mononuclear phagocyte. A few eosinophils were noted, and neutrophilic granulocytes were rare, forming less than 1 per cent of the exudate. At points at which exudate was most profuse, edema was also more prominent, and myocardial fibers showed swelling, longitudinal fragmentation, and loss of striations. Phagocytosis of the injured fibers was present in these areas. No endocardial lesion was noted, and the only change found in the epicardium was an infiltration of lymphocytes adjacent to the myocardium of the left ventricle and right atrium. Vascular changes were not noted except for one small, recently thrombosed vein. In the lungs edema was prominent, with many mononuclear phagocytes, scattered neutrophils, and eosinophils within the alveoli and interstitial tissues. Numerous plaques of hyaline material were deposited upon the alveolar walls in the lower lobes. Hyperemia was marked. No bronchial or pulmonary vascular changes of note were found.

In the liver, evidence of mild hyperemia was present, and many of the hepatic cells were swollen, with poor cytoplasmic detail, and with areas of fatty vacuolization and pyknosis. Some edema was present in the spaces of Disse. No frank necrosis was found. In the spleen, lymphoid follicles were hyperplastic, and approximately 50 per cent had central necrosis. The only changes noted in the gastrointestinal tract were an unusual prominence of lymphoid follicles. The adrenal glands were well preserved and without evidence of necrosis or lipid exhaustion. In the kidneys there were foci of hyperemia. Hyaline thickening of the basement membrane of the glomeruli could be found regularly, with slight proliferation of endothelium and an occasional focus of epithelial activity in Bowman's capsule.

Case 3

This 1 year old white male infant was admitted to the North Carolina Baptist Hospital because of dyspnea and elevation of temperature. He had been well until 48 hours earlier when progressive respiratory difficulty developed and he was admitted to an outside hospital. He became cyanotic shortly before admission there. Intercostal retraction was noted, but heart sounds were regular and apparently strong. Eighteen hours later, after transfer, signs of consolidation were present over the right base, heart sounds were difficult to evaluate, and the liver was palpable 3 cm. below the costal margin. The white blood cell count rose from 19,000 to 27,000, with 74 per cent neutrophils in each instance. A test for albumin in the urine was 1 plus, and there were 2 white blood cells and 2 red blood cells per high power field. On roentgen examination of the chest the cardiac silhouette was markedly enlarged. Penicillin, Aureomycin, chloramphenicol, and aminophylline were administered successively. The child was in the fluoroscopic room preparatory to pericardial paracentesis when he died suddenly, approximately one hour after admission.

At autopsy cyanosis of the face and head was evident externally. Approximately 60 cc. of clear yellow fluid was present in each pleural cavity, but none in the other serous cavities. The heart weighed 100 Gm. (normal, 44 Gm.). The left ventricle in particular was dilated, and on section the myocardium was mottled, pale, and flabby. The lungs were heavy, the right weighing 145 Gm. (normal, 64 Gm.) and the left 65 Gm. (normal, 51 Gm.). There was an unusual and diffuse firmness throughout each lung, without evidence of localized consolidation. The liver was slightly enlarged, with irregular mottled hyperemia. The spleen was not enlarged, but malpighian bodies were unusually prominent. No gross changes were found in the kidneys, adrenal glands, or gastrointestinal tract.

Microscopic examination showed an irregularly diffuse infiltration of lymphocytes, large mononuclear phagocytes, and occasional plasma cells. No eosinophils were present, and neutrophils were rare. The myocardial fibers in the areas of focalization showed more evidence of degeneration, with fragmentation and nuclear pyknosis, than was found in the less involved areas. Edema was present throughout the entire myocardium. The reaction was perhaps more evident in the outer one-half of the myocardium and in the septum than in the zone adjacent to the endocardium. No endocardial inflammatory changes were found. The epicardial lesion consisted of an infiltration in the deep layers by the same cells which were present throughout the heart.

In the lungs, hyperemia was prominent, with edema, neutrophilic granulocytes, and large macrophages in the alveoli. The spleen was hyperemic, with prominent follicles, necrotic at their centers. Edema and fatty change were moderate in the liver. No changes were found in the intestinal tract. Glomerular lesions were similar to those described in case 1.

Case 4

This 10 month old female had a "head cold" which persisted for about one week, following which treatment—probably a sulfonamide drug—was administered, resulting in improvement in three to four days. Edema involving the hands, legs and abdomen, and associated with a decrease in urinary output, occurred approximately one week later. The child was admitted to Duke Hospital, because of rapid breathing, three weeks before death. On physical examination, the temperature was 37.3 C. (99.2 F.), pulse 180, respiration 48, blood pressure 104 systolic, 66 diastolic. There was edema of the legs and sacrum, and, to a lesser degree, of the face and arms. The heart was not enlarged and no rales were present. The liver was palpable 11 cm. below the costal margin.

The accessory clinical findings included a white blood cell count which varied between 16,000 and 19,000, with a normal differential. The hemoglobin was 8.1 Gm. Examination of the urine gave the following results: specific gravity, 1.030; protein, 1 plus; 0 to 10 white blood cells, and 1 to 2 granular casts. Nonprotein nitrogen ranged from 26 to 34 mg. per 100 cc. The total serum protein was 5.6 Gm. per 100 cc., with an albumin-globulin ratio of 3.1:2.5. The electrocardiogram showed sinus tachycardia. On the second day the blood pressure rose to 250 systolic, 200 diastolic, and then fell to normal within the next 36 hours. The temperature, which was slightly elevated, returned to normal at about the same time.

The patient was digitalized, with resultant improvement in pulse and a loss of about 1 kg. in body weight. Upon general improvement she was discharged after two weeks. She returned six days later because of "cold" of two days' duration, vomiting, and rapid breathing. The temperature was 38 C. (100.6 F.), pulse, 160, respirations, 80. The heart was enlarged and manifested a gallop rhythm, and the liver was also enlarged. The child was acutely ill, and died approximately 36 hours after admission.

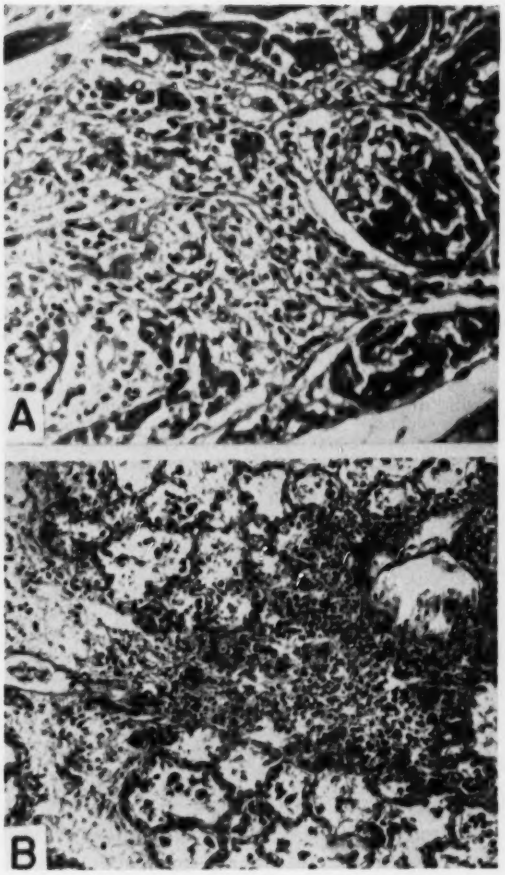

Fig. 4. (Case 4) A. A focus of degeneration with relatively slight inflammation in the heart. In other areas the inflammatory reaction was predominant. B. The focal inflammatory reaction and interstitial edema in Case 4. The hyaline alveolar plaques are not shown here.

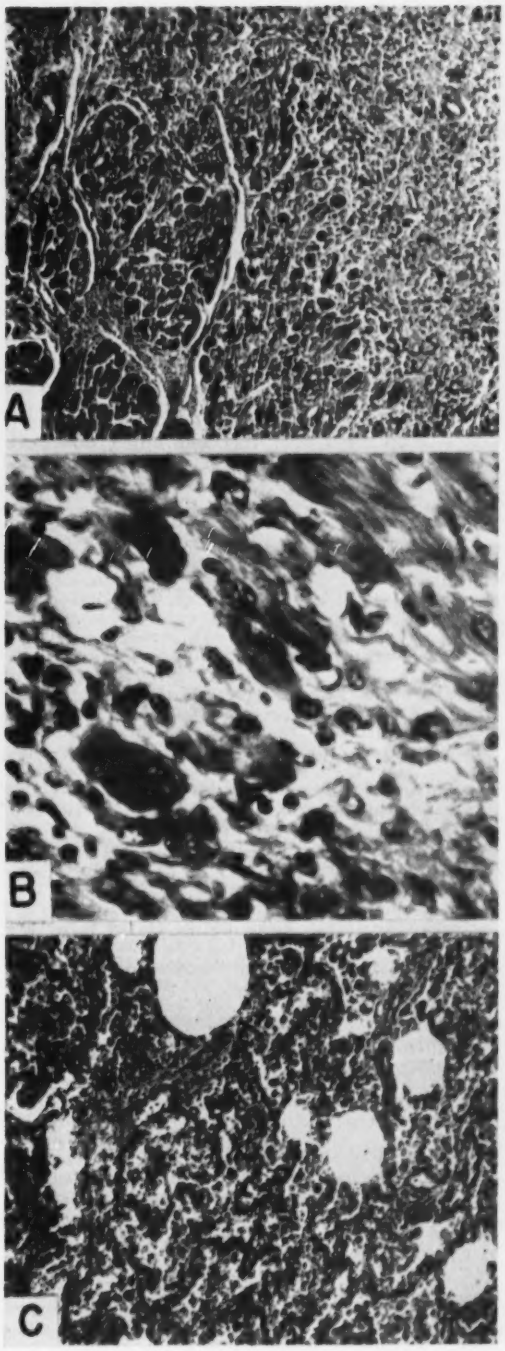

Fig. 5. (Case 5) A. The border of a large necrotic area. Scattered giant cells can be seen at this power. B. A higher power photomicrograph to show the necrotic myocardial fibers and the formation of the symplastic giant cells. C. The changes in the lung, with partial collapse, alveolar phagocytes, and the interstitial changes in the alveolar walls are shown here.

Autopsy disclosed some edema of the thighs and legs, and a small amount of fluid in the pleural and pericardial cavities, but none in the peritoneal cavity. The heart weighed 90 Gm. (normal, 34 Gm.), and was both hypertrophied and dilated, particularly the left ventricle. The lungs were edematous, the right weighing 40 Gm. (normal, 49 Gm.), and the left weighing 150 Gm. (normal, 41 Gm.). The spleen weighed 50 Gm. (normal, 19 Gm.), and was hyperemic, with unusually prominent lymphoid follicles. The gastrointestinal tract and pancreas showed no lesions. The liver weighed 440 Gm. (normal, 227 Gm.), and was markedly hyperemic. The kidneys were enlarged, weighing 40 and 45 Gm. respectively (normal, 30 Gm.).

Microscopically, the heart showed a striking interstitial infiltration of lymphocytes, mononuclear phagocytes, plasma cells, and eosinophilic and neutrophilic granulocytes, occurring more or less diffusely, with focal accentuations. The lesion was perhaps more severe in the inner one-third of the myocar-

dium, and was associated with diffuse edema extending into the atria, where relatively slight inflammatory exudate was present. In the ventricles there were foci of necrosis of the myocardial fibers, with phagocytosis by large mononuclear cells. Fibroblastic activity in these necrotic areas was minimal, the impression of increased density being due mainly to collapse of the supporting connective tissue. Myocardial fibers in areas other than the foci of frank necrosis, showed pyknosis, and fragmentation, both longitudinal and transverse. This change was not universal, but occurred more or less focally. The endocardium was involved only in areas adjacent to the more severe inflammatory reaction in the myocardium. The epicardium was not involved, nor was there evidence of a primary vascular injury nor accumulation of exudate about the vessels. In the lungs edema was prominent, involving the alveolar walls and the alveolar spaces. Central lobular hyperemia and some cloudy swelling was present in the liver. In the kidney many glomeruli showed thickening and some hyalinization of the basement membranes, with slight proliferation of endothelium and prominence of the cells lining Bowman's capsule. No tubular lesion was evident. Hyperemia was prominent.

Case 5

This 11 year old white boy was admitted to Duke Hospital, three days before death, with nausea and vomiting of four days' duration. Investigation indicated that he had been dyspneic on exertion for several weeks. No history of exposure or intercurrent infection was obtained. He was given small white divided tablets by his family physician, without improvement. When it was discovered that he had an enlarged heart, he was referred to the hospital. On admission the blood pressure was 80 systolic, 60 diastolic, pulse 150, weak and irregular, respirations 30, temperature 38.8 C. (102 F.). The child was weak and ill, with cyanosis of the lips and nails. The heart was enlarged, and the liver was palpable three fingerbreadths below the costal margin. The spleen and kidneys were palpable.

Laboratory data: There were 4,380,000 red blood cells per cubic millimeter, with 12 Gm. of hemoglobin, 11,900 white blood cells with 72 per cent polymorphonuclear neutrophilic granulocytes, and 5 per cent stab forms. Examination of the urine disclosed a specific gravity of 1.028, with occasional white blood cells and epithelial casts. The nonprotein nitrogen rose to 90 mg. per 100 cc. The heart rate became irregular and rapid, increasing up to 200 per minute. The patient died on the third hospital day.

At autopsy cyanosis of the lips and nailbeds was present. Eight hundred cubic centimeters of clear yellow fluid was found in the right pleural cavity, 200 cc. in the left pleural cavity, 300 cc. in the pericardial cavity, and none in the peritoneal cavity. The heart weighed 235 Gm. (normal, 116 Gm), and was flabby and dilated, with soft yellow areas beneath the trabeculae carnae of the left ventricle. The left lung weighed 370 Gm. and the right 390 Gm. (normal, 177, 116 Gm.). The posterior aspects of the lungs were red and noncrepitant. The spleen was not enlarged, weighing 75 Gm. It was dark and soft, with prominent malpighian bodies. The liver was somewhat enlarged, weighing 980 Gm. (normal 850 Gm.). It was dark red, with small, mottled darker hyperemic areas beneath the capsular surface. The intestines showed no lesions, but the mesenteric nodes were slightly enlarged. The kidneys were not enlarged, but were moderately hyperemic.

Microscopically, large areas of necrosis in the myocardium contained an inflammatory exudate consisting of lymphocytes, plasma cells, mononuclear phagocytes, and rather numerous eosinophilic granulocytes. Degeneration in many of the myocardial fibers was complete, and the fibers had disappeared in the more severely involved areas. At the borders of some of the larger lesions, however, fragments of muscle fibers remained, undergoing phagocytosis by large mononuclear cells. In addition to these foci, large sheets of lymphocytes were present in the interstitial areas beneath the epicardium. Muscle cells in these areas also showed evidence of injury. Scattered through almost all of the larger foci of necrosis were giant cells of the syncytial or symplastic type, apparently formed from muscle fibers. In a few instances these large multinucleated cells could actually be demonstrated within myocardial fibers which retained their cross-striations. In other fibers the nuclei were swollen and hyperchromatic, particularly at the borders of the necrotic areas. Other similar nuclei lay within clumps of slightly granular neutrophilic cytoplasm, rather sharply outlined and apparently ameboid in character. Still others were present within eosinophilic masses, sometimes with surrounding myofibrils evident in cross section. Other giant cells were of more usual types, some resembling foreign body giant cells and others the Langhans type. There was no evident endocardial injury other than in areas lying immediately adjacent to the myocardial lesions. Here, recent mural thrombi were attached.

The lungs were markedly hyperemic and edematous, with numbers of mononuclear phagocytes within the alveoli and slight extravasation of the red blood cells. No pneumonia could be found. The spleen was hyperemic, with prominent lymphoid follicles, some of which showed central necrosis. No lesions were noted in the other organs. In the kidneys there was swelling of the glomerular basement membrane, less than in other cases. Some edema fluid was found in the glomerular spaces, and there was proliferation of the epithelium of Bowman's capsule. No tubular disease was noted.

Comment

In each of these 5 cases the illness was of short duration, less than three days in the first 3 and of questionable duration in the latter 2. Case 4 was marked by severe edema and an episode of hypertension, suggesting glomerulonephritis clinically. The use of one of the sulfonamide drugs is probable but not definite in this case. The history in the other cases does not indicate whether medication was used in the distant past, except that in case 5 the use of sulfonamide medication was denied. A common factor in the first 4 cases was an upper respiratory infection during the terminal illness. In the fifth case, the boy is said to have been dyspneic on exertion for several weeks, but a history of preceding respiratory or other possible contributory illness was not obtained.

In all cases, an enlarged heart was found on physical examination in the stage preceding death. In 2 cases cardiac enlargement had not been noted earlier in the illness. Temperature elevation was not strikingly high, but pulse and respiratory rates were elevated, and the pulse was "thready" and

weak in all cases. There was slight to moderate leukocytosis.

At autopsy the heart was enlarged to approximately twice its normal weight in all cases, and usually all chambers were dilated. The myocardium was flabby and grayish-tan or mottled. In case 5, large areas of necrosis were present in the left ventricle. Pulmonary edema and hyperemia were present in all, and interstitial pneumonia was found in the first 3, with some alveolar exudate in case 2. In this case the lungs were firm and rubbery, with deposits of hyaline material upon the alveolar walls. Pneumonia was not a striking factor, however, in any of these cases. The lymphoid follicles of the spleen were prominent, and in all cases there was extensive necrosis of germinal centers. Hepatic lesions were those of recent passive hyperemia.

Renal glomerular changes consisting of swelling of the basement membrane, occasional splitting, and hyaline thickening were found in each case. This change was occasionally confined to one or two lobules, but it was more usual to find the entire glomerulus involved, with alterations in the axial segments and in the capillary walls. Endothelial proliferation was evident in some capillaries of each glomerulus, but occlusion of the lumen was not noted. Epithelial cells lining Bowman's capsule were prominent. No direct injury to the blood vessels was found, though in case 5 there were rare wedge-shaped areas of fibrosis and lymphocytic infiltration in the cortex, probably of vascular origin. The glomerular changes were most prominent in the child who had experienced edema and an episode of hypertension 10 to 12 days before death (case 4). These lesions were similar to, but more severe than those in other cases. No evidence of tubular disease was recognized in any of these 5 cases.

In 2 cases, the heart's blood was sterile. The myocardial lesion was not recognized, and the tissue was not cultured. In 2 autopsies performed in outside hospitals, no bacteriologic studies were done. In case 5 alpha hemolytic streptococci and *Escherichia coli* were isolated from the lungs and myocardium, but not from the blood of the heart. Studies of sections of lung and myocardium in all cases stained by the MacCallum method did not reveal the presence of organisms.

We have no etiologic suggestions to offer in any of these cases except perhaps that of the 11 year old boy from whose heart and lungs alpha hemolytic streptococci were isolated at autopsy. It seems that this organism should not be dismissed lightly, although the reaction in the heart is not considered usual in infections produced by this organism. Schenken and Coleman[22], and Schenken and Heibner[23] have reported 2 cases of myocarditis in which a micro-serophilic streptococcus was isolated and considered of etiologic significance. It is known that the streptococcus may produce an inflammatory reaction with a prominent mononuclear component rather than the fulminating infection characterized by edema and granulocytic neutrophilic response. It would seem that a continuing injury to the myocardium is probable either as a result of direct bacterial injury or through the development of hypersensitivity, in view of the presence of this organism in the wall of the left ventricle and in the lungs at the time of autopsy. The development of necrosis was probably followed by the histiocytic exudate, and indeed phagocytosis was continuing and active at the time of death.

The formation of giant cells as a part of this reaction is somewhat more difficult to explain, except as a reaction to altered tissue proteins and lipids in the instance of those giant cells of the Langhans and foreign body types. The syncytial cell masses formed from muscle cells may be regarded as an element in the process of repair similar to the symplastic giant cells which occur at times in voluntary muscle following injury. Forbus[47] has shown in experimental studies on voluntary muscle that they may arise from the collapsed sarcolemma, or through mitotic division of the nucleus. In the myocardium, swelling of nuclei, hyperchromatism and occasionally mitotic figures could be found in cells whose cytoplasm had retained or developed striations demonstrable in phosphotungstic acid prepartions. Saphir[4] has described and illustrated giant cells of this type in what has been termed "granulomatous myocarditis." Other instances of "giant cell myocarditis" and "granulomatous myocarditis" have been noted and in one case reported recently by Kean and Hoekenga[58], asteroid bodies were found within the giant cells. In none of those instances was an etiologic agent discovered, despite careful search.

The glomerular alterations have not been

described in other reports of myocarditis. They are definite though mild, and are apparently reversible. Case 4 is the exception in this group, being marked by more severe glomerular injury. Such lesions are found in instances of circulatory and pulmonary insufficiency, and are not considered significant in clarifying the nature of the myocarditis.

Until more thorough and adequate bacteriologic and virus studies are made at autopsy following recognition of the lesion in fresh material, we can expect little clarification of this type of "isolated myocarditis." When the changes are recognized under the microscope, the opportunity for such studies has passed.

The broad spectrum of etiologic agents reviewed here suggests that many instances of myocarditis could be removed from the "isolated" group and classified more specifically. The term "isolated myocarditis" is still useful to indicate the occurrence of myocardial disease in the absence of other recognized specific disease processes.

Summary

1. The many etiologic possibilities in myocarditis have been reviewed.

2. Five cases of myocarditis in children are reported. In 4, no etiologic explanation is offered, while in the fifth a hemolytic streptococcus was isolated from the heart and lungs at autopsy and was thought to have been of etiologic significance.

3. Glomerular lesions were noted in all cases. In 4 they were minor; in one the injury was more severe, and apparently not reversible.

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MYOCARDIAL CHANGES IN DERMATOMYOSITIS*

Report of a Case

JOSEPH MENDELOFF, M.D.

FAYETTEVILLE

Dermatomyositis is included in the category of collagen diseases[1]. Although this classification provides a necessary pigeonhole, it serves no useful purpose. The etiology and pathogenesis remain completely unknown. It is not a disease of skin and muscle alone, but a systemic disorder. Whereas some cases are clear cut, others are difficult to distinguish from lupus erythematosus.

The case to be reported was marked by significant histologic changes in the heart. The purpose of this paper is to present a description of these changes with some comment.

Case Report

When first seen, the patient was a 28 year old Negro grocery clerk. He was hospitalized twice at our institution. The first admission was for a period of 156 days; the second admission occurred one year later and lasted 89 days.

First admission

The patient complained of generalized malaise, symptoms of an upper respiratory infection, and intermittent fever for about three weeks prior to admission. There was some dermatitis, with recent involvement of the left upper eyelid.

A skin disorder of the face had started four years previously, with scaly lesions of the scalp producing alopecia and erythematous scaly lesions on each side of the face. During the intervening years pustules had appeared around the zygomatic areas, which gradually dried up but maintained a scaly crusty appearance.

On admission the patient was fairly well developed. There were no abnormal findings of the heart or lungs. The blood pressure was 100 systolic, 60 diastolic. The liver and spleen were not palpable. There was superficial dermatitis of the left upper eyelid. Other lesions of the scalp and face were described as inactive scars, with loss of pigment.

Throughout his hospital stay his white count was usually about 5,000, with 69 per cent polymorphonuclears, 25 per cent lymphocytes, and 6 per cent monocytes. On one occasion he had 5 per cent eosinophils. The hemoglobin dropped from 14 to 7.5 Gm., and eventually rose to 12 Gm. (Sahli). Hematocrit levels dropped from 41 to 28, and then rose to 41. Liver function studies never disclosed any abnormal findings. Blood chemistry determinations were always within normal limits. Urinalyses showed a good range of specific gravity, and albuminuria varied from negative to 2 plus. The Fishberg concentration was 1.013, 1.016, and 1.018. Several examinations of bone marrow and peripheral blood for L. E. cells were negative.

Roentgenograms of the chest showed a slight increase in the size of the heart. Five electrocardiographic examinations were reported as within normal limits.

The patient had erratic temperature fluctuations ranging from 99 to 105 F. Toward the end of this hospitalization his temperature receded to below 100 F. On admission he weighed 117 pounds; when he left the hospital he weighed 114 pounds.

He received a course of ACTH (without particular benefit).

After 156 days he left the hospital on a pass and failed to return.

Histologic examination of skin specimen: The surface was covered with some fibrillar keratotic and parakeratotic material. The epidermis was reduced to layers of three to four cells, and rete pegs were virtually absent. There was edema of the cutis and dilatation of capillaries. In the upper corium was a fine brown pigment, most of which was free and some contained within round and elongated cells. (This pigment proved to be negative for iron, but could be bleached by nascent chlorine.) There were scattered small areas of necrosis in the corium, and necrobiotic nuclear material was present.

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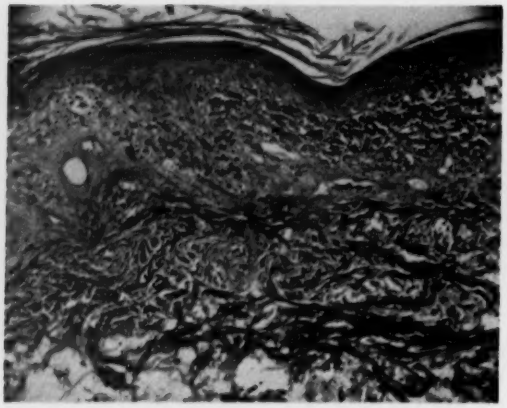

Fig. 1. Photomicrograph of skin during first admission showing epidermal change, type and distribution of cellular infiltration in the corium, with alterations of collagen. (X 140).

The remainder of the corium consisted of moderately dense connective tissue (fig. 1). These findings were considered consistent with a diagnosis of lupus erythematosus. Examination of an epitrochlear lymph node on the left indicated a reactive hyperplasia.

Second admission

One year later the patient returned with a history of weight loss, malaise, afternoon fever, loss of appetite, and skin disorder of both forearms. These symptoms were of two months' duration.

On admission the blood pressure was 90 systolic. 60 diastolic, and the pulse 104. He appeared chronically ill and debilitated. There were depigmented areas of the scalp with thinning of the hair, and scaly lesions at the side of nose and left upper eyelid. On the wrists and forearms were areas 1 to 3 cm. in diameter of dry, scaly, slightly raised dermatitis. The anterior and posterior chest wall showed areas of increased pigmentation. The heart sounds were normal. There was a slight generalized lymphadenopathy. The liver and spleen were not palpable. The patient had three anal fissures.

The white cell and differential counts showed no significant variations (4,000 to 7,000 white cells). No eosinophilia was ever present. The hemoglobin fell from 13 Gm. on admission to 9.5 Gm. Hematocrit fell from 42 on admission to 26. There was a constant albuminuria of 3 to 4 plus. Granular and hyaline casts with 2 to 6 red blood cells per high power field were seen occasionally. Specific gravity varied from 1.012 to 1.026. Five examinations of peripheral blood for L. E. cells were reported as negative. The total serum protein was 5.6, albumin 2.4, and globulin 3.2. All other blood chemical determinations were within normal limits.

Roentgen studies on one occasion disclosed the heart to be moderately enlarged; but on previous and subsequent examinations it was reported normal in size. Cardiograms on this admission showed abnormalities which were not present previously. The electrocardiogram showed inverted T1 and TV5 and V6, with some coving of the ST segments in these leads. The limb leads showed borderline low voltage and a sinus rate of 124. Several weeks later, a second degree 3 to 1 auriculoventricular block with a ventricular rate of 62 developed. The T waves were inverted in leads 1, 2, and 3, AVL, AVE, and V2, V3, V4, V5, and V6. Approximately four days later the patient's rhythm was sinus, with a rate of 102, a PR interval of 0.14, and a normal QRS conduction. T waves were again inverted in 1, 2, AVL, V4, V5, and V6. Electrocardiograms taken during the remainder of his hospital stay were essentially the same until the time of his death.

The temperature varied between 102 and 103 F. Toward the end he had normal and subnormal temperatures. There was a persistent tachycardia, with rates of 120 and occasionally a gallop rhythm. A month after admission he was digitalized and given ACTH. Both drugs were continued up to the time of death. The patient became markedly cachetic, and paronychia and decubitus ulceration developed. He died on the eighty-ninth day of his second hospitalization.

Histologic examination of the skin taken from the left forearm showed the surface to be covered by a very thin layer of parakeratotic material. The layer of surface epithelium was narrow, and there were no rete pegs or papillae. The corium was composed of loose fibrillar connective tissue. The diagnosis was atrophy of the skin.

Postmortem examination—gross

The body was that of a 30 year old Negro man. There was a marked degree of cachexia. Numerous discrete and confluent crusted elevated pigmented areas were present over both arms and legs, some of which were ulcerated. On the thorax and trunk was a fine,

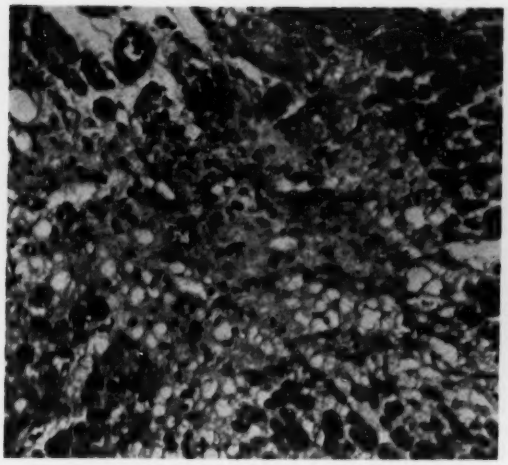

Fig. 2. A focal lesion in the myocardium showing loss of muscle cell substance and round cell infiltration. (X 254).

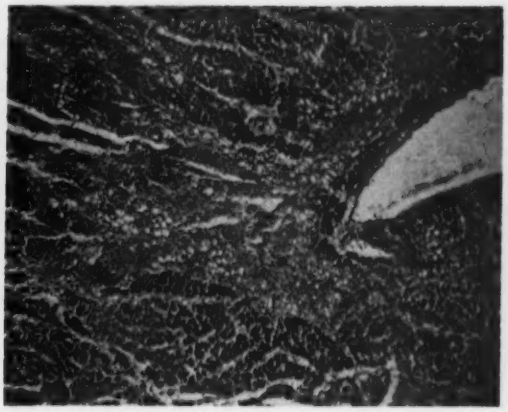

Fig. 3. A focal lesion in the myocardium showing necrosis and loss of muscle cell substance with a polymorphonuclear cellular response. (X 81).

hyperpigmented speckled discoloration of the skin. Crusted ulcerated lesions were present over the scalp and face. There were two completely depigmented white areas over the face.

Subcutaneous fat was minimal. The voluntary muscles were a very pale reddish-brown, considerably reduced in size, and had a pseudogelatinous appearance.

There was no free fluid in the body cavities, the linings of which were smooth and shiny. Mesenteric lymph nodes measured 1 cm.; on section they were soft and gray. Periaortic lymph nodes at the level of the renal arteries and lower measured 1 to 3 cm. in size. They were firm and, on section, dull brown in color.

The heart weighed 260 Gm. The myocardium was pale red, uniform, and firm. There were no abnormalities of the valves or coronary arteries.

There were no abnormalities of the remaining viscera. The liver weighed 1,330 Gm., the spleen 120 Gm., the left kidney 180 Gm., the right kidney 179 Gm., and the brain 1,300 Gm.

Postmortem examination—microscopic

Sections from the left ventricle and interventricular septum revealed focal necrotic changes of groups of muscle cells. In some places muscle fibers had disappeared completely, leaving only the framework of the muscle with scattered inflammatory cells throughout the area (fig. 2). Other groups of muscle cells were replaced by hyaline eosinophilic material. In still other areas, necrosis of muscle cells had occurred and polymorphonuclears, nuclear fragments, and granular eosinophilic material were present (fig. 3). Other changes consisted of slight interstitial edema and slight hyaline thickening of occasional intramyocardial arteries. Rare arteries showed slight perivascular infiltrations of lymphocytes and monocytes. The epicardium contained some short bundles of dense staining collagen and some scattered round cells.

Skin from the chest and knee showed similar changes. The surfaces were covered with varying amounts of parakeratotic material. The epidermis was thin, and was composed of two to three layers of squamous cells. Such rete pegs as were present were small and delicate. Some cells of the basal layer contained increased pigment; others, none. Collagen in the upper corium was dense in some places, granular in others. There were small numbers of stellate cells containing brown pigment, and also some sparse perivascular collections of lymphocytes. Collagen bundles in the deeper layers were coarse, and there were also some widely dilated vascular channels. Small arteries in the subcutaneum showed proliferation of the intima and moderate degrees of thickening of the walls (fig. 4).

Sections of the pectoral muscle revealed marked changes in both the muscle cells and interstitium. The muscle fibers showed vascular disintegration, hyaline necrosis, and

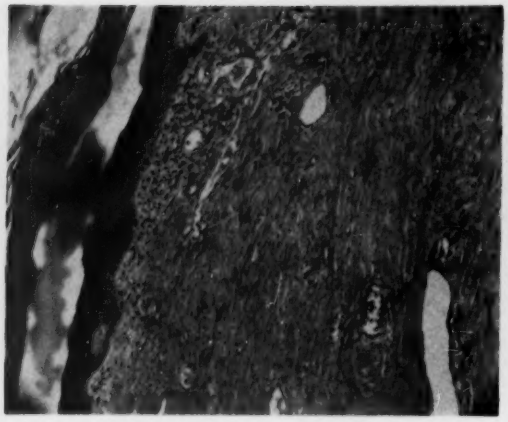

Fig. 4. Skin from chest (postmortem) showing epidermal atrophy, round cell infiltration, dilated vascular channels, and density of the corium. (X 140).

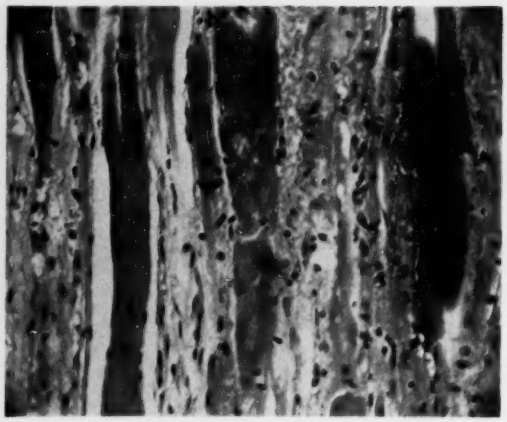

Fig. 5. Pectoral muscle showing degenerative and necrotic changes of muscle cells with interstitial reaction. (X 254).

complete destruction. They also varied in width, some being shrunken and atrophic, others swollen. In some places proliferation of nuclei formed small linear basophilic clumps (fig. 5). The interstitial changes consisted of scattered dense collections of lymphocytes, small areas of necrosis occupied by lymphocytes, and polymorhonuclears (fig. 6)

Other changes were interstitial edema and, in some places, the presence of loose fibrillar to dense connective tissue between muscle cells. Small arteries and arterioles showed moderate degrees of thickening of their walls, and a fair number were surrounded by very dense collections of lymphocytes and occasional polymorphonuclears. There were a few instances of round cell infiltration within the walls of these vessels.

The fat around periaortic nodes consisted of numerous large pale polygonal cells with granular cytoplasm. In several places were clumped deposits of calcium. Elsewhere were many interstitial eosinophilic fibrils with infiltration of lymphocytes, monocytes, and occasional polymorphonuclears and eosinophils.

Glomeruli contained a slight but distinct hyaline swelling of the basement membranes. In an occasional glomerulus, a loop of the tuft was swollen and necrotic, and contained nuclear fragments and polymorphonuclears. The basement membrane of an occasional tubule showed some thickening and hyalinization. Blood vessels did not show any changes.

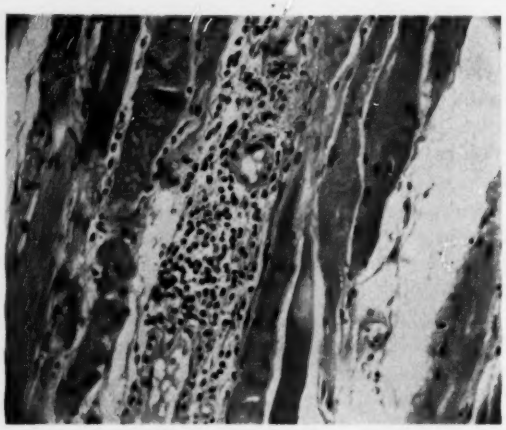

Fig. 6. Pectoral muscle showing muscle changes similar to those demonstrated in figure 3. The interstitium contains a dense round cell infiltration. (X 254).

The lungs showed small focal areas of atelectasis and small focal areas of lobular pneumonia.

The spleen was unremarkable.

No abnormalities consistent with congestive heart failure were observed in the lungs, liver, or pancreas.

Comment

O'Leary and Waisman[2] have reported an analysis of 38 cases, 19 of which ended fatally. Among the 38 patients there was a decrease in blood pressure; 9 patients presented objective evidence of clinical heart disease; 4 showed abnormal electrocardiographic findings. In cases reaching autopsy,

the findings in the heart were said to be similar to those found in the voluntary muscles. O'Leary[3], in a general review, stated that myocarditis with hypertrophy and cardiac failure was an occasional cause of death in this disease.

In an attempt to correlate clinical cardiac manifestations with postmortem findings, I have reviewed 15 cases with autopsies, 14 from the recent literature[4] and the case being reported. It soon became apparent that recorded cases were not as complete as could be desired. Both clinical and pathologic data relating to the heart were often not included, so that one could not determine whether certain factors were normal or had not been noted.

The ages in the group ranged from 7 to 76 years. Tachycardia was present in 4 cases, blowing systolic murmurs in 3 cases, extrasystoles in 1 case, and gallop rhythm in 1 case. Blood pressure usually varied from low to normal. There were no instances of significant hypertension. No report other than our own made mention of signs or symptoms of congestive heart failure. A diagnosis of congestive heart failure was made in the case I have reported, and the patient was digitalized. If he had had congestive heart failure, then either the treatment was effective or the demand on the heart was very slight, for at postmortem there were none of the classic findings which are associated with congestive heart failure. Seven cases had abnormal electrocardiograms; one case was reported normal, and the remaining reports made no mention of such observations. The changes reported consisted of low voltage, depressed and inverted T waves, coving of ST segments, extrasystoles, and tachycardia. The most that can be said about these findings is that they are nonspecific and are indicative of myocardial damage.

None of the 15 case reports described any significant gross abnormalities of the heart. There were no cases with enlarged hearts. All the reports, however, mentioned or described microscopic changes in the heart. These consisted of focal and diffuse interstitial edema, atrophy, fragmentation, degeneration, and necrosis of muscle cells, focal inflammatory reactions consisting of lymphocytes and in some cases polymorphonuclears, and occasional perivascular collections of cells. No significant changes of small intramyocardial vessels were noted. Some measure of fibrosis was found in 3 cases; the respective ages of these patients were 13, 27, and 49 years.

It thus appears that in this disease there are no remarkable gross changes in the heart. If anything, the hearts are small and share in the loss of weight which accompanies the severe cachexia. Microscopic findings are quite variable and, for the most part, are focal in distribution. Some cases have slight findings, such as interstitial edema. At the other end of the scale, there are severe necrotizing lesions of muscle cells with varying responses of inflammatory cells. The nature of these changes is nonspecific and analagous to those seen in the skin and voluntary muscles.

Summary

An attempt to correlate clinical and postmortem findings in the heart in cases of dermatomyositis has been made.

One case is described in detail and 14 others are reviewed.

It would seem that there are occasional nonspecific clinical signs of heart disease. Electrocardiographic abnormalities are more common, but they too are nonspecific. No cases demonstrating satisfactory evidence of congestive heart failure were found. Focal microscopic lesions in the myocardium are common, varying from mild lesions, such as edema, to violent necrotizing lesions.

Nothing about the lesions in any part of the body gives any clue to the pathogenesis of this disease. Although the abnormalities are widespread and systemic, they are nonspecific.

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MYOCARDIAL ABSCESS

Case Report

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RALEIGH

The diagnosis of myocarditis has changed radically within the past several years from the "chronic myocarditis" that had come to be included on the death certificate of most older patients. This change has come about through the insistence on acceptable evidence of true inflammation of the myocardium, most frequently through demonstrable morphologic changes.

Some clinicians have maintained that true myocarditis is a fairly common disease, and that its frequency and importance has not been fully appraised. In the light of more complete and accurate studies of pathologic material, it seems now that the condition is not such a rarity, and the pathologist not infrequently must convince the clinician of its existence and its primary role in the cause of death. These discrepancies are doubtless due to difficulties in recognizing myocarditis clinically, except when it is known to be frequently associated with, or a complication of certain conditions resulting in specific functional changes.

In analyzing material from 5,626 autopsies in the Michael Reese Hospital, Chicago, excluding cases of contagious disease, Saphir encountered myocarditis in 240 cases, or 4.26 per cent. In his subdivision of the forms encountered, one group of 32 cases represented abscesses in the myocardium not related to endocarditis. The bacteriologic findings in these cases are not known, but Saphir quoted bacteriologic data from 26 of 31 cases of myocardial abscess from the department of pathology of the Boston City Hospital. The causative organism was *Staphylococcus aureus* in 20 cases, pneumococcus in 2, *Streptococcus viridans* in 2, *Streptococcus pyogenes* in 1, and meningococcus in 1. In all cases of bacteremia myocardial abscess might be expected.

The following case, although illustrating the major role of a myocardial abscess in the death of the patient, is usual not only in the probable sequence of events, but in the bacteriologic agent, which at its present state of identity is considered a saphorphyte.

Case Report

The patient was a 50 year old white man who had bilateral saphenous ligations for varicosities of both lower extremities, and phlebitis of the superficial veins of the right leg. On the thirteenth postoperative day he experienced sudden acute pain radiating from the back to the left upper part of the abdomen. His temperature rose sharply to 104 F, and leucocytosis doubled to 19,000 per cubic millimeter, with 80 per cent neutrophilic polymorphononuclears. Roentgen examination of the chest revealed no evidence of embolic phenomena, and the heart was normal in size and outline. His temperature subsided to normal after 48 hours, but following discharge he did not return to work because of general malaise and weakness of the lower extremities.

Approximately six months later he began complaining of frontal headaches, which became progressively more severe. About one month later, while talking to friends, he suddenly clutched his right hand and lapsed into unconsciousness, from which he never recovered during the remaining 17 days of life. At this time roentgen examination of the chest showed the lung fields to be clear, but the heart "somewhat enlarged," and an electrocardiogram recorded T waves of low amplitude. No murmurs or abnormal sounds were heard. The patient's temperature varied between 100 and 101 F, and blood pressure averaged approximately 120 systolic, 80 diastolic until the day before death, when the temperature rose to 104 F and blood pressure to 144 systolic, 80 diastolic.

An autopsy performed a few hours later disclosed, in summary, an abscess located near the extreme apex of the heart with part of a mural thrombus attached to the endocardium of the left ventricle over this area, a cerebral abscess 8 cm. in diameter involving the left frontal and left parietal areas, thromboses in several branches of the superior mesenteric artery with hemorrhagic necrosis of a large part of the ileum and jejunum, an organized thrombus almost completely occluding the right axillary artery, and, finally, a large embolus recently detached from the mural thrombus partially wedged into and occluding the innominate artery.

When the pericardial sac was opened, a quantity of lemon-yellowish purulent exu-

date was encountered, samples of which were taken for bacteriologic examinations. On removal of this exudate, however, the epicardium and inner lining of the pericardial sac appeared smooth, with the exception of a point of attachment between these two surfaces near the extreme apex. Separation of these structures revealed an abscess partially outlined proximally by fibrous tissue, but no hemorrhagic reaction or evidence of recent infarction. On the endocardial surface corresponding to this region a friable but fairly well organized thrombus was attached to the wall of the left ventricle. The remaining endocardium was smooth throughout, the valves and orifices appeared competent, and no vegetations could be found.

The coronary arteries showed mild to moderate sclerosis, with some eccentric narrowing, but no occlusions could be demonstrated except in the immediate vicinity of the abscess. Multiple sections of the myocardium showed small areas of fibrosis grossly. These were noted microscopically, but no other specific characteristics were recognized. There was extensive myocardial degeneration including swollen fibers with loss of striations and some loss of staining reaction, round cells, and a few polymorphononuclear leucocytes diffusely infiltrated the interstitial tissue. In the vicinity of the abscess, mononuclear cells with numerous phagocyte cells were seen, although polymorphonuclears were not conspicuous.

Gram negative bacilli were demonstrated in sections from the region of the myocardial abscess and from the material from the brain abscess.

Bacteriologic examination of the exudate identified the organism as a gram-negative non-motile bacillus producing a lemon-yellowish pigment on several media and representing a member of the Flavobacteria. Attempts to identify this organism further have been unsuccessful as yet, but in all available references it is classified among the environmental bacteria. Its origin or mode of entry in the foregoing case is not known, but its causal relationship appears established, after the development of an abscess in the myocardium, with subsequent formation of a mural thrombus in the left ventricle providing a source of emboli. The duration of the myocardial abscess cannot be determined with certainty, perhaps emphasizing some of the difficulties of a clinical diagnosis, but some enlargement of the heart was noted after a period of seven months. The dramatic episodes of probable embolic nature preceding the patient's second hospitalization strongly suggest the presence of the mural thrombus in the left ventricle at this time, although the brain abscess might well have antedated this. Furthermore, it does not seem unlikely that phlebitis in the right lower extremity provided the mechanism or means of entry of this bacterium, which was of such low or questionable virulence that its presence was not otherwise manifested.

Interest has recently been renewed in the effort to identify further this organism following its recovery in a blood culture from another patient who has had repeated myocardial infarctions over a period of several years. In addition to biologic studies for identification, sensitivity tests against several of the antibiotics were undertaken, and the bacterium was found to be highly sensitive to the antibiotic used in therapy. Repeated blood cultures made subsequently were negative. Ironically, one of the antibiotics that showed no inhibition *in vitro* against this organism was the only one used in the treatment of the myocardial abscess reported above.

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MYOCARDIAL FIBROSIS*

OSCAR DUQUE, M.D.

DURHAM

It is generally admitted that the large majority of cases of myocardial fibrosis result from coronary arteriosclerosis. Occasionally, however, the pathologist is confronted with the problem of explaining extensive myocardial fibrosis in hearts that present little or no coronary sclerosis. In these cases, cardiac failure may or may not have been present, and no direct cause of myocardial injury may be evident at the time of autopsy. The present study attempts to review briefly some of the factors which may produce fibrosis of the myocardium in the absence of coronary sclerosis.

The Question of Myocardial Regeneration

Myocardial fibrosis does not result from

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the mere proliferation of fibrous tissue. In the myocardium, fibrosis must be preceded by the destruction of muscle fibers. This postulate brings out the question: Does the cardiac muscle regenerate? If it does, one would expect that focal, limited areas of myocardial destruction should heal by regeneration of the fiber, and fibrosis should not develop.

This point of view was adopted early by Heller[1]. In his pioneering studies he came to the conclusion that regeneration of myocardial fibers did indeed occur and was an important factor in the healing of toxic degeneration of the myocardium. His opinion found support in the work of Warthin[2], who described the presence of mitosis in diphtheritic myocarditis. The longitudinal splitting, terminal swelling, and the presence of an occasional mitosis described by Heller were taken again, more recently, as suggestive of myocardial hyperplasia (King)[3]. These observations, and those of many others, were immediately contested. Karsner[4] found no evidence of true regeneration of muscle in the healing of experimental myocardial infarct. He also cites the work of Aschoff, Loeb, Christian, Smith and Walker, who did not think that regeneration occurred in the healing of cardiac injuries. The work of these investigators has established what appears to be today the general consensus—namely, that injured myocardial fibers do not possess the power to regenerate in a significant degree. When destruction of more than a microscopic area of myocardium occurs, healing takes place by proliferation of connective tissue and fibrosis.

An especially interesting aspect of this problem is the regenerative potential of the heart muscle of infants. McMahon[5] points out the rarity of myocardial scarring, after injury, in infants. He studied the hearts of children with cardiac hypertrophy and one case of diphtheria in which mitoses were present in the myocardium. From his studies he concluded that in cardiac hypertrophy in infants proliferation of heart muscle fibers can take place, and that in severe myocardial injury in children regeneration of myocardial elements can occur. These results are supported by Mallory[6], who also believes that in very young children there is a general hyperplasia of cardiac muscle elements following injury.

One point of special significance related

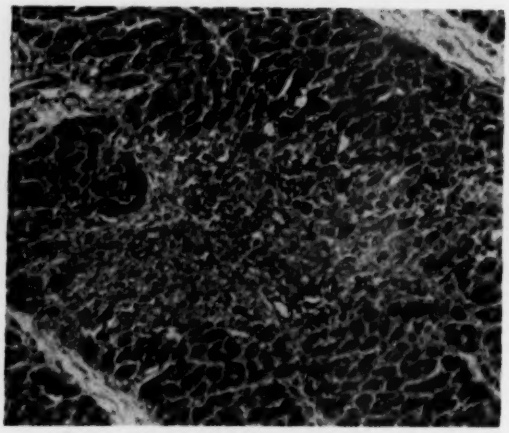

Fig. 1. Photomicrograph showing a focal area of inflammation and necrosis in myocardium. Necrotic fibers have disintegrated. Connective tissue proliferation will form here a fibrous scar. Hematoxylin and Eosin. (X 171).

to the problem of myocardial regeneration deserves emphasis here. Focal degeneration of myocardial fibers occurs in almost any severe illness. Thus it is not rare to find focal areas of cloudy swelling, fatty degeneration, edema, and hyalinization of muscle fibers in patients dying with high fever. Scarring of the heart in the absence of coronary sclerosis, however, is not as frequently seen as the common occurrence of myocardial degeneration in disease might suggest. Myocardial fibers must then possess the power to recover completely following sublethal injury. It is not known at what stage a degenerative myocardial lesion becomes irreversible. Ring[7] suggested that the abortive attempts at regeneration which he observed in experimental myocardial infarctions were due to the absence of a sarcolemmal framework along which the new fibers might grow. A corollary to all these considerations is that the lesion of myocardial destruction heals largely by proliferation of connective tissue elements with scar formation.

The background of myocardial scarring is, then, myocardial destruction. This occurs to a greater or lesser extent in a large number of diseases of varied nature. It is not within the scope of this presentation to review all those diseases in which myocardial degeneration and sclerosis have been described. The discussion will be limited to those commonly occurring pathologic conditions which

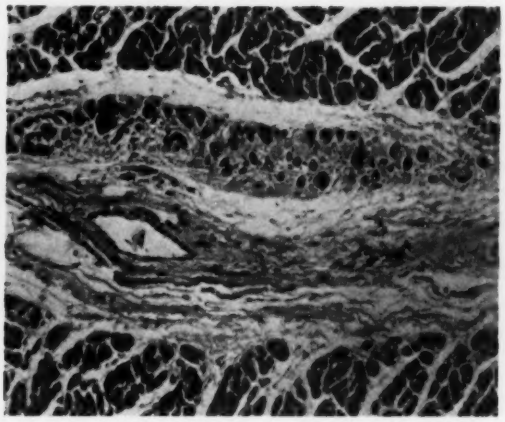

Fig. 2. Acute rheumatic myocarditis. A fibrous scar involving myocardium, forming about a healing Aschoff body. Hematoxylin and Eosin. (X 140).

are known to cause or to be accompanied by myocardial damage.

Inflammatory Disease with Myocardial Injury

Rheumatic fever

Damage to the myocardium in rheumatic fever is referable to three mechanisms: (1) direct rheumatic myocardial injury, (2) interference with myocardial circulation resulting from arteritis, and (3) coronary circulatory failure due to valvular disease.

In most cases of acute rheumatic fever the lesion is essentially interstitial; little damage is produced to the myocardial fiber. This was the original view as expressed by Aschoff[8]. Rich and Gregory[9] described small foci of myocardial necrosis which they did not find in the less severe form of rheumatic myocarditis. I have found no difficulty in demonstrating focal areas of muscular necrosis in the vicinity of Aschoff nodules. Another type of injury to muscle in this first group is the trapping and destruction of myocardial fibers by scar tissue in the vicinity of a healing rheumatic nodule. It must be recognized, however, that diffuse myocardial fibrosis is not usually due to acute rheumatic myocarditis except in those cases in children in which the disease has been rather severe. Five of our cases studied at autopsy in which a past rheumatic carditis had been established clinically but in which there was no residual valvulitis showed only a minimal degree of focal scarring.

In the second group, injury is produced by circulatory disturbances caused by rheumatic arteritis. The mechanism here is then comparable to the slow obstruction of the coronary arteries by arteriosclerosis.

Rheumatic valvulitis may produce scarring of the myocardium through hypoxia resulting from disturbances in the total coronary circulation due to valvular inefficiency or, through hypoxia of individual fibers, to insufficient blood supply consequent to fiber hypertrophy.

Bacterial myocarditis (myocarditis in bacteremia)

Bacteria circulating in the blood stream may lodge and colonize in the heart, producing acute myocarditis. Routine sections of the right and left ventricle in 14 cases of fatal septicemia were reviewed. These cases were not complicated by chronic renal disease or hypertension, chronic pulmonary disease, coronary sclerosis or long-standing illness. The etiologic agents in these 14 cases were: streptococci 3, staphylococci 4, pneumococci 2, meningococci 2, *Hemophilus influenzae* 1, *Escherichia coli* 2. In 3 of the cases there had been clinical symptoms of myocarditis, but no endocarditis was described clinically or at autopsy. Two of the cases with clinical symptoms of myocarditis presented a diffuse inflammatory infiltrate and focal areas of muscular necrosis. In the remaining cases, 3 showed discrete foci of inflammation which in 2 of the hearts were accompanied by focal areas of necrosis. Extensive necrosis or fibrosis was not present in any of the 14 cases. Endocarditis may be accompanied by myocardial injury caused directly by the organism responsible for the valvular infection, or it may produce infected emboli which in turn cause infected infarcts or foci of suppuration.

Myocardial damage associated with pneumonia

Although myocarditis with clinical manifestation is not a frequent complication of pneumonia, pathologic anatomic evidence of myocardial damage in this disease is not rare. Stone[10] studied 34 cases of lobar pneumonia and 37 instances of bronchopneumonia. He found an interstitial myocarditis in 2.9 per cent of the cases with lobar pneumonia. In 8.9 per cent of all cases he found more discrete inflammatory infiltrates.

In the present study 10 cases of lobar pneumonia (pneumococcus) were reviewed.

Lesions were found in the hearts of 7 of the patients. In 2 of these there were scattered focal areas of necrosis of muscle. A diffuse interstitial infiltrate with poly- and mononuclear leukocytes was found in 1 of the 7 cases. Focal inflammatory infiltrates were present in the remaining 4 cases; all 7 hearts presented also focal areas of edema and cloudy swelling of the myocardium. Of 10 cases of lobular pneumonia, 5 presented some degree of focal interstitial inflammation in the heart. One of these 10 cases presented scattered myocardial necrosis associated with hemorrhage.

Myocardial damage in viral disease (poliomyelitis)

Numerous reports of myocarditis in poliomyelitis have appeared in the literature. Ludden and Edwards[11] found myocarditis in 14 of 35 autopsy cases. I have studied routine autopsy slides of the hearts of 9 patients dying of poliomyelitis. In 3 of these cases there were focal scattered areas of inflammatory exudate, some of them associated with focal myocardial necrosis. Of these 3 cases, 1 patient died of massive aspiration pneumonia, and 2 had been living in a respirator for several days; the lungs of these 2 patients presented extensive areas of bronchial pneumonia. Pulmonary infection is a frequent complication of poliomyelitis. The role of pneumonia in the production of the myocardial lesions found in poliomyelitis deserves further study. Schmidt[12] has reported the isolation of a virus from a chimpanzee dying of myocarditis which produced myocarditis in mice, hamsters, and guinea pigs. He pointed out the similarity of lesions in these experimental animals to those described in the cases of poliomyelitis with myocarditis.

Diphtheria

Myocardial changes in diphtheria have attracted a great deal of attention. Warthin[2], and Gore[13] have emphasized the presence of varying degrees of parenchymatous degeneration associated with inflammatory changes. Extensive myocardial fibrosis may occur after diphtheritic myocarditis (Mönckeberg)[14]. Seventeen autopsy cases were reviewed for the present studies. Severe myocarditis with necrosis was present in 1 of the cases; in another, there was a focal, scattered inflammatory infiltrate and severe swelling of the muscle fibers, but there was no myocardial necrosis. A mild degree of edema was found in the remaining 15 cases.

Syphilis

According to Warthin[15], syphilis is one of the commonest causes of myocardial fibrosis. Nevertheless, the occurrence of a true syphilitic myocarditis has been greatly disputed. It is generally admitted today that myocarditis in syphilis must be extremely rare. When it occurs, fibrosis of the myocardium in patients with syphilis is probably related indirectly to syphilitic aortitis.

Myocardial Injury in Nutritional Disturbances

Beri-beri

Clinical symptoms of cardiac impairment are frequent in this disease. Histologically, the changes are degenerative, characterized by edema and vacuolar degeneration (Mebius)[16]. Wenckebach, quoted by Wartman and Hill[17], described also a form of liquefactive degeneration (sarcolysis). Wartman and Hill[17] stated that there may be also a slight degree of scarring.

Potassium deficiency

Myocardial degeneration and necrosis can be produced in rats by diets deficient in potassium[18]. Myocardial injury produced by dietary deficiency in man probably never occurs. Electrocardiographic evidence of cardiac damage is present in pathologic states associated with potassium depletion (dehydration in children). Potassium deficiency can be artificially induced in man and animals by the administration of desoxycorticosterone acetate[19]. Goodof and McBryde[20] reported necrosis and inflammation in the myocardium of a patient with Addison's disease treated with desoxycorticosterone.

Myocardial Injury in Diseases Peculiar to Muscle and Connective Tissue

Extensive scarring was observed by Nothacker and Netsky[21] in the myocardium of 6 patients with progressive muscular dystrophy. A case of myasthenia gravis, studied by Dr. Dillon at Duke Hospital, presented scattered, focal areas of myocardial necrosis. The sarcoplasm of the involved fibers had completely disappeared, while the sarcolemmal nuclei seemed to have proliferated, giving to the lesion a pseudogranulomatous appearance. A similar change was not found in the heart in 4 other cases of myasthenia,

although a few small foci of necrosis were present in 1 of these hearts. No lesions were found in the hearts of 2 children with amyotonia congenita studied in Duke Hospital.

Extensive myocardial fibrosis probably does not develop in lupus erythematosus. However, Humphreys[22] found small scars resembling small infarcts in the hearts of 21 patients who had this disease. More important appear to be the myocardial lesions in scleroderma. Extensive myocardial scarring was found in 2 cases of Weiss[23], and in the case of East and Oram[24].

Hypoxia, Hypertension, and Uremia

It may be advantageous to consider these three factors together because of their interrelations in causing diffuse myocardial scarring. Diffuse myocardial scarring in a case of chronic renal disease with hypertension, anemia, and uremia provides a classic example of this interrelationship. It is well known that fatty degeneration of the myocardium is found frequently in severe anemia. Friedberg and Horn[25] have described discrete areas of necrosis of cardiac muscle in patients dying of severe anemia. Uremia, in the absence of hypertension and arteriolitis, is probably of no importance in the production of myocardial fibrosis. In our material no significant lesions were found in 12 cases of uremia not accompanied by hypertension, arteriosclerosis, or arteriolonecrosis. Five of these were cases of glomerulonephritis; 4 patients died with the syndrome of lower nephron nephrosis, and the remaining 3 cases were, respectively, bilateral kidney infarct, bilateral cortical necrosis, and acute mercurial intoxication. Similar results were reported by Clawson[26].

A relative degree of myocardial hypoxia[27] may be the cause of myocardial scarring in hypertension, when the heart is both dilated and hypertrophied. Hypoxia may be the dominant factor in cardiac hypertrophy and dilatation produced by valvular disease of any etiology. Hypertension alone probably does not produce significant myocardial damage. A case of Cushing's disease and one of pheochromocytoma of the adrenal gland, both with hypertension but without coronary sclerosis, did not reveal any significant myocardial lesions. When hypertension and uremia are associated for a long time, as in chronic renal disease, discrete areas of myocardial degeneration and necrosis are often found (Gouley)[28].

Idiopathic Myocarditis

This discussion cannot be concluded without mentioning the so-called isolated or Fiedler's myocarditis. At present, these terms include all those lesions of the myocardium of unknown etiology, consisting of myocardial necrosis, leukocytic exudate, histiocytic, and sarcolemmal proliferation giving to the lesion a pseudogranulomatous appearance. Extensive destruction of heart muscle is found in this type of myocarditis, and usually is fatal. Healing of the lesions to the extent permitted by the short duration of the disease results in scattered areas of fibrosis.

Summary

From the preceding discussion, which is based upon observations made on groups of fatal cases of myocardial failure in 7,000 autopsies, and from a survey of the pertinent literature it is clear that in the absence of coronary sclerosis myocardial fibrosis may be the result of many etiologic types of myocardial injury which produce an effect common to all—namely, necrosis of heart muscle and its supporting tissues. The most common and most important of these injuries are briefly reviewed.

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TUBERCULOUS MYOCARDITIS*

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DURHAM

Tuberculosis of the myocardium is an uncommon entity. Gore and Saphir[1], in reviewing 1,402 cases of myocarditis, found that tuberculosis accounted for only 9. These were found in a group of 581 patients who died of tuberculosis. Three forms of the myocardial disease are usually described[2]: (1) nodular (the nodules attaining at times such a size as to cause cardiac embarrassment[3]; (2) miliary; and (3) diffuse infiltrating. The occurrence of these three types is usually accepted. The existence of a fourth variety has been the subject of controversy for some time[4].

The major problem in almost all cases is that, unless the disease is detected grossly in a heart, no cultures are made. When the microscopic changes suggest tuberculosis, the heart is usually so well fixed that cultures are not possible. Even the finding of acid-fast bacilli in a lesion is not absolute proof that the disease is tuberculous, although such evidence is rather strong. What of those cases in which the individual has every evidence of tuberculosis elsewhere and has a granulomatous process in the heart? Admittedly, the evidence is purely circumstantial, but it is in accord with the commonly accepted technique of attempting to explain as many findings as possible on the basis of a single entity.

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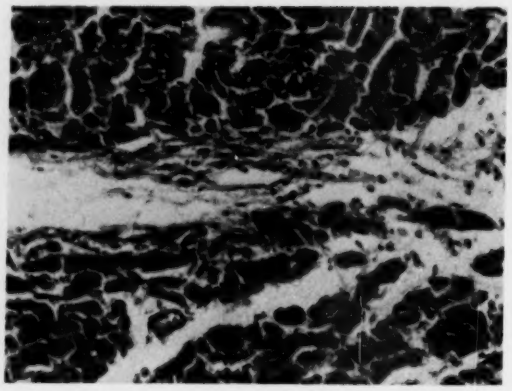

Fig. 1. Case 1. A fusiform collection of spindle-shaped cells in the interstitial tissue of the heart. The collagen appears thickened, but there is no necrosis. (X 200).

The following cases are reported not to solve any of the foregoing problems, but to present examples of granulomatous myocarditis observed in patients with tuberculosis.

Case 1

A 26 year old Negro woman was admitted to the hospital 12 days before death because of excessive enlargement of the abdomen during pregnancy. She went into premature labor and died shortly after delivery. There had been no evidence of any myocardial disease. On physical examination the only observation of importance was a harsh systolic murmur over the heart. The blood pressure was 118 systolic, 58 diastolic. At autopsy a tubercle measuring 3 mm. in diameter was found on the endocardial surface of the left ventricle 1 cm. beneath the aortic valve. Elsewhere throughout the myocardium were small grayish flecks. The remainder of the organ showed a generalized disseminated tuberculosis, with the largest lesion appearing in the left upper lobe. On microscopic examination, in addition to the endocardial tubercle mentioned above, there were small foci of cellular infiltrate which resembled Aschoff bodies (fig. 1). Such areas consisted of foci of mononuclear cell infiltrate. No acid-fast bacilli were found in these lesions, although they were seen rather readily in many of the other sections of tissue.

Case 2

This patient was the child prematurely delivered in case 1. The child was born at eight months gestation and lived for a period of six hours. In the placenta rather numerous tubercles were seen. The lymph nodes within the abdomen were enlarged, and there was a generalized tuberculosis in many of the organs. There were two unusual foci in the heart. One consisted of a small focus of mononuclear cells with multinucleated giant cells, but without caseation (fig. 2). The other was a perivascular focus of mononuclear reaction associated with a thrombus.

Case 3

A 3 year old colored girl was admitted to the hospital because of intermittent fever of one year's duration and an abdominal mass of 3 months' duration. There was no history of cardiac symptoma-

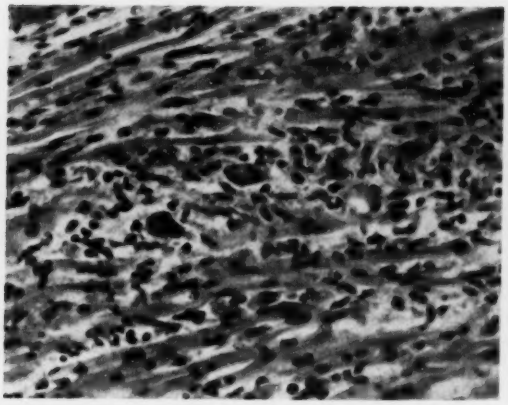

Fig. 2. Case 2. Focal area of mononuclear cell infiltrate separating myocardial fibers. Note absence of necrosis and presence of two Langhans type giant cells. (X 400).

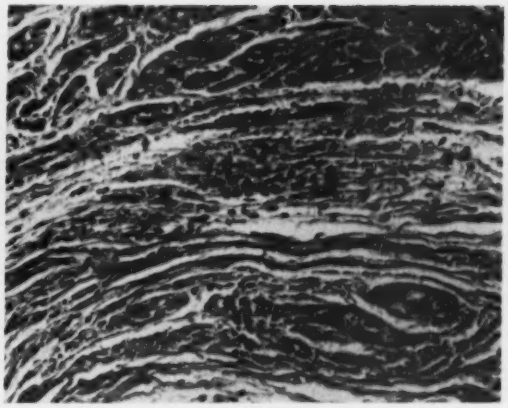

Fig. 3. Case 3. Aschoff-like body occurring at base of right ventricle between endocardium and myocardium. A similar focus appeared several millimeters distant in the myocardium. (X 200).

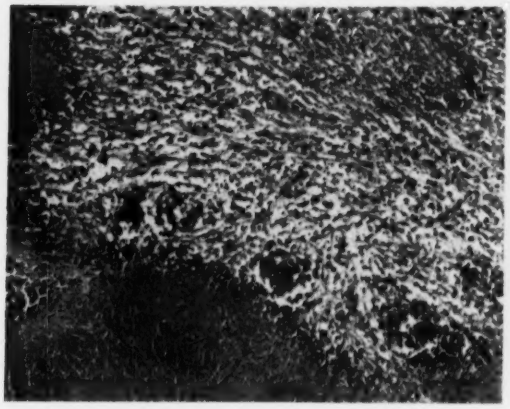

Fig. 4. Case 4. Large mass of caseous necrosis extending through the myocardium. (X 120).

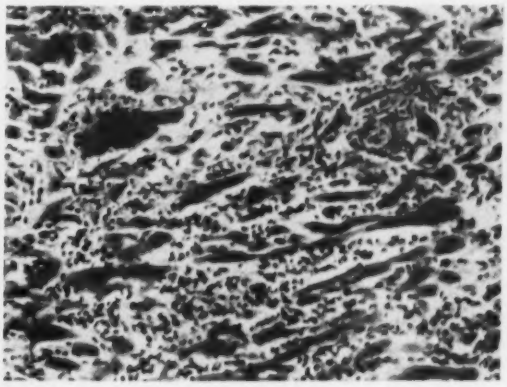

Fig. 5. Case 5. One well formed and one poorly formed microscopic tubercle are seen. No caseation is evident. (X 200).

tology. At autopsy there was generalized tuberculosis. The primary lesion was thought to be in the abdomen. In the heart of this patient also there were seen the small foci of mononuclear cell reactions described above. In this instance the reaction more closely resembled Aschoff bodies than in case 1 (fig. 3).

Case 4

A 25 year old colored man was admitted to the hospital with meningitis. In this patient, as in cases 1, 2, and 3, there was no history of myocardial disease. His course subsequent to admission was one of gradual deterioration. At the time of autopsy it was found that the disease process involving the heart began as a mediastinal lymphadenitis. One of these lymph nodes had eroded into the pericardial cavity. A tuberculous pericarditis had developed. The process had then extended through the myocardium and endocardium. The endocardial lesion ulcerated, and in this way a generalized hematogenous dissemination occurred. The microscopic lesions in the heart were characteristic of tuberculosis with caseous necrosis (fig. 4). The myocardial disease in this instance was thought to be related to the direct extension from the lymph node rather than by hematogenous dissemination.

Case 5

A 35 year old Negro woman was admitted to the hospital complaining of dizzy spells of three months' duration. For four years she had had a dry, unproductive cough associated with some dyspnea. It was found that she had a cavity in the lung, and treatment by pneumothorax was instituted. Her Wassermann reaction at the time of admission was 4 plus. At the time of autopsy the right ventricle of the heart was dilated and hypertrophied. Throughout the myocardium of both ventricles, there were diffuse, small, yellowish patches. In the lungs, as was suspected clinically, there was fibroid tuberculosis, with cavity formation. Also within the lungs were areas of tuberculous pneumonia. The heart showed extensive areas of granulomatous inflammation without, however, evidence of caseation. The most well formed tubercles are seen in figure 5. Elsewhere there was a diffuse and focal lympho-

cytic and occasional monocytic infiltrate. Acid-fast bacilli were not demonstrated within the lesions in the heart.

Comment

The case of direct extension of a granulomatous process into the myocardium (case 4), would be acceptable as a case of tuberculosis of the myocardium.

Cases 2 and 5 present a more difficult situation. The patients had a definite tuberculous infection elsewhere in the body, and the appearance of the granulomatous inflammation in the heart would lead one to suspect that this was likewise tuberculous. The absence of acid-fast organisms by microscopic examination makes the diagnosis a little uncertain. Another factor which might be considered in case 5 is, of course, the 4 plus Wassermann reaction. Lesions similar to those seen in this patient have been described in syphilis. The patient noted as case 2 was a newborn whose mother had a negative serologic reaction for syphilis. The child, therefore, had no likelihood of a syphilitic infection.

More interesting problems are raised by cases 1 and 3. In case 1, there is a focus where the endocardial lesion has extended into the heart, and in such an area one would have no difficulty in accepting a tuberculous origin for the disease. Elsewhere in the heart, however, as illustrated in the photograph, are unusual lesions which are similar to those found in case 3. In both cases there is incontrovertible evidence of tuberculosis elsewhere in the body. In the heart, such evidence or definite evidence is lacking. The lesions seen are foci of mononuclear cell infiltrate not associated with multinucleated giant cells and appearing in the absence of caseation. To my knowledge, the first description of such lesions was made by Masugi, Murasawa, and Ya[4]. Yamada[5] also reported similar findings. The question raised by these authors and by the present author is: Is this lesion a manifestation of tuberculous myocarditis? Yamada came to the conclusion that this lesion was related to tuberculous allergy[5]. Such a conclusion seems to be justified. The patients would, without doubt, exhibit altered reaction to the tubercle bacillus. This reaction would probably be better classified as a hypersensitivity. The source of the tubercle bacilli producing this response would, of course, be the blood stream. The patients described above would all have at one time or another tubercle bacilli within the circulating blood.

The foregoing discussion is not meant to imply that rheumatic fever and tuberculosis are similar diseases. The implication is only that one may see in the heart of patients with tuberculosis lesions which are suggestive of Aschoff bodies in rheumatic fever.

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SARCOIDOSIS OF THE MYOCARDIUM*

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The myocardium is not infrequently involved in cases of disseminated sarcoidosis. The lesions of sarcoid in the myocardium were first described by Bernstein and others in 1929[1]. Their case showed sarcoid lesions in the epicardium and myocardium, but there was no evidence that these lesions produced any abnormality of cardiac function. Later reports, however, have shown that myocardium sarcoidosis can be a fatal disease, and Yesner and Silver[2], in a review of the literature, found death attributed directly to sarcoidosis of the myocardium in 9 of 13 cases examined at autopsy. Some of these cases were examples of sudden death resulting from the myocardial sarcoidosis.

In their recent monograph, Longcope and Freiman[3] have shown that sarcoid of the heart occurs in about 20 per cent of the cases examined at autopsy. These lesions vary from one or two scattered sarcoid tubercles to a widespread destructive process involving large areas of myocardium. Such lesions may cause changes in cardiac function either by involvement of the conduction system of

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the heart or by direct destruction of myocardium. Most of the cases of sudden death due to myocardial sarcoid have been attributed to ventricular fibrillation or to Stokes-Adams syndrome[2]. Other cases with extensive myocardial damage have ended in chronic congestive heart failure from myocardial insufficiency[2].

At least 21 instances of myocardial sarcoidosis are recorded in the literature. Longcope and Freiman listed 18 cases, but stated that in the Johns Hopkins Hospital series there were 3 other cases which showed a few myocardial lesions[3]. This brings the total number to 21.

The purpose of this report is to record the clinical and autopsy findings in 4 new cases of myocardial sarcoidosis. These cases came from the autopsy material of Duke Hospital. Sections were stained with hematoxylin and eosin, Wilder's stain for reticulum fibers, Kinyoun's stain for acid-fast organisms, MacCallum's stain for bacteria, and the Hotchkiss-McManus stain for fungi.

Case Reports

Case 1

A 46 year old Negro man was seen in the Outpatient Clinic eight years before death complaining of occasional palpitation and mild asthmatic attacks with dyspnea and orthopnea. Diagnoses of bronchial asthma and hypertensive cardiovascular disease were made. Four years before death, in 1943, the patient was admitted to the hospital complaining of asthma with dyspnea and orthopnea, swelling of the ankles, and some precordial pain. The blood pressure was 170 systolic, 110 diastolic. Exudates were present in the ocular fundi, and there was cardiac enlargement. The total serum protein was 6.8 Gm., with 4.3 Gm. globulin, 2.5 Gm. albumin, and an albumin-globulin ratio of 0.58.

The patient improved on digitalis therapy, but after discharge the cardiac and asthmatic status became worse. He entered the hospital for the second time in 1947, a few days before death, in congestive heart failure. Blood pressure of 190 systolic, 116 diastolic, a palpable liver and ankle edema were observed. The hemogram was normal. A roentgenogram of the chest showed a generalized process of some kind radiating outward from both hilar regions. The patient was improving, but two days before death an electrocardiogram revealed a ventricular rate of 76, an auricular rate of 118. There was sagging of the S-T segments, and the T waves were inverted. This was interpreted as complete heart block, with intraventricular rhythm. The patient died suddenly of unexplained cause on the fourth hospital day.

At autopsy the unexpected finding was Boeck's sarcoidosis of the lungs, pleura, trachea, pericardium, auricular myocardium, superior vena cava, pulmonary veins, mediastinal and axillary lymph nodes, left supraspinatus muscle, kidneys, and liver.

Gross examination of the heart revealed small gray nodular elevations studding the area around the base of the heart on the parietal pericardium. There were some small gray nodules on the surface of the right auricle, most of which were about 1 mm. in diameter, and the auricles in some areas measured 1 cm. in width. The ventricles did not show this change. The heart weighed 600 Gm., and showed hypertrophy and dilatation. Numerous small nodular areas were seen in the lungs and the lymph nodes of the mediastinum.

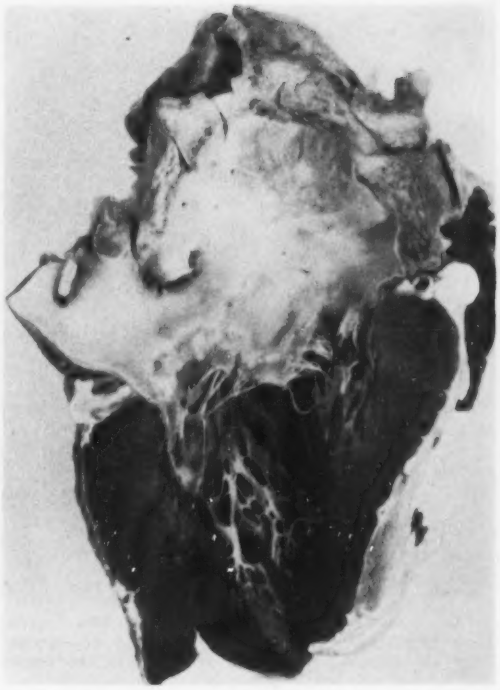

Fig. 1. Photograph of heart in case 1, showing sarcoid nodules involving the auricular myocardium.

On microscopic examination, the auricle of the heart showed a granulomatous process which had infiltrated and destroyed muscle fibers, and also involved the pericardial fat, but which had spared the endocardium. This process was composed of numerous epithelioid cells which frequently formed epithelioid tubercles. Langhans' giant cells were also present in the tubercles. These small tubercles showed no caseation. The walls of the great veins were also involved in a similar granulomatous process. The lungs showed considerable fibrosis and contained numerous scattered epithelioid tubercles, with Langhans' giant cells. The lymph nodes showed extensive infiltration with numerous hard tubercles. Several characteristic Schaumann bodies were seen in the giant cells. Special stains for acid-fast organisms, bacteria and fungi were negative.

Case 2

A 27 year old Negro woman entered the hospital complaining of dyspnea and a productive cough of two months' duration. Two years before admission she had had migratory joint pains involving most of the joints and accompanied by some fever. These symptoms lasted for three months. About six months prior to admission, the patient began to have exertional dyspnea and anorexia, and lost some weight. The symptoms became progressively worse.

On physical examination she was orthopneic. There were moist rales of both lungs and some en-

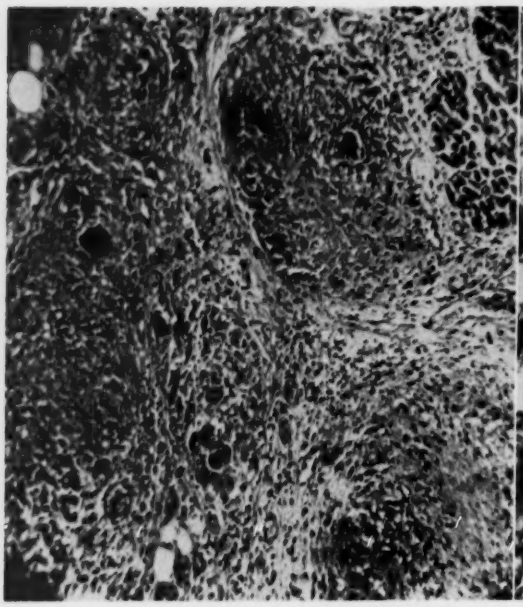

Fig. 2. Section of auricle in case 1. The sarcoid granulomas have replaced much of the myocardial tissue. A few muscle fibers are seen in the upper right. (X 160).

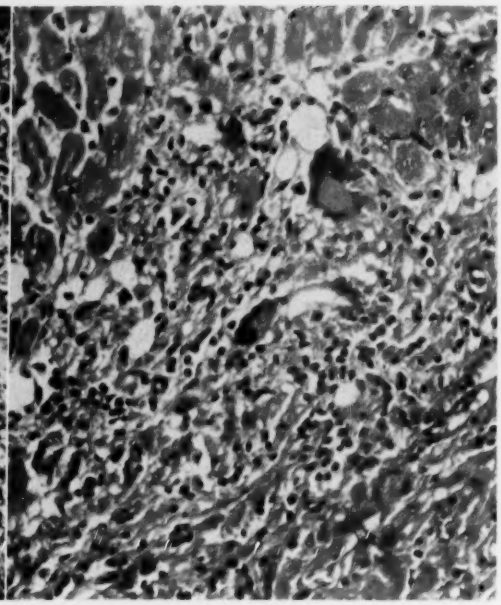

Fig. 3. Ventricular myocardium in case 2, showing a small irregular granuloma associated with some fibrosis. (X 300).

gorgement of the neck veins. The heart was enlarged and a systolic murmur was heard at the apex. The liver was enlarged, and there was shifting dullness in both flanks. The hemogram showed a slight anemia. Sputum examination was negative for acid-fast bacilli. The tuberculin skin test was negative. Electrocardiographic studies produced a record consistent with myocardial damage, although there was normal sinus rhythm. Chest roentgenograms showed a small mass in the right upper mediastinum. The patient did not respond to therapy and died 34 days after admission.

At autopsy granulomatous lesions forming epithelioid tubercles involving the myocardium, mediastinal, hilar and cervical lymph nodes, lungs, liver, spleen, kidneys, and thyroid were found.

On gross examination, the heart weighed 320 Gm., and all chambers were dilated. Scattered through the myocardium, especially in the ventricular walls, was a patchy scarring. There was a fresh mural thrombus in the left ventricle, and a few small tubercles 1 mm. in diameter were found in the lungs. The mediastinal, hilar, and cervical lymph nodes were enlarged, with small granulomatous lesions in which no caseation was found.

On microscopic examination the heart showed extensive fibrosis, and scattered through the fibrotic areas were several irregular tubercles consisting of a few round cells and giant cells of the Langhans' type. The tubercles were widely distributed. There were typical epithelioid tubercles in the lungs, associated with some fibrosis, but never with evidence of caseation. Similar tubercles were found in the liver, spleen, kidneys, and the thyroid gland. Numerous special stains were negative for all organisms.

Case 3

A 22 year old Negro woman entered the hospital with palpitation and recurrent epigastric pain of four days' duration. Physical examination revealed a blood pressure of 100 diastolic, 80 systolic, engorged neck veins, and a pulse rate of 165 over the precordium. There were a few shotty cervical lymph nodes. There was no evidence of congestive failure.

A hemogram was normal. The electrocardiogram indicated a ventricular tachycardia, rate 180, with QRS complexes characterized by predominant negative deflections in all leads. Notched, slurred, and widened QRS complexes were present in all leads. The impression was ventricular tachycardia consistent with some underlying myocardial disease. Chest films showed an increase in diffuse linear markings throughout all lung fields and tremendous enlargement of the hilar lymph nodes on both sides. This was thought to be consistent with Boeck's sarcoid. The patient was started on quinidine therapy. The heart rate slowed to around 90, but the patient died suddenly 10 hours after admission.

Autopsy revealed a granulomatous process composed of epithelioid tubercles involving the myocardium and mediastinal lymph nodes, with scattered hard tubercles throughout the lungs, liver, and spleen. At gross examination the heart weighed 225 Gm. On cut surface there was a firm, yellowish-white tissue partially replacing the muscle of the left ventricle and extending almost completely throughout the wall in some areas. The lungs weighed 620 and 720 Gm. Throughout the lungs were multiple small nodules, 1 mm. in size and yellowish-white in color. The mediastinal lymph nodes were enlarged. On cut surface they showed a nodular consistency.

On microscopic examination the heart exhibited a diffuse granulomatous inflammatory process composed of epithelioid cells, small round cells, and giant cells, with an increase in fibrous connective tissue. This process occupied about three fourths of the wall of the left ventricle. Scattered throughout the

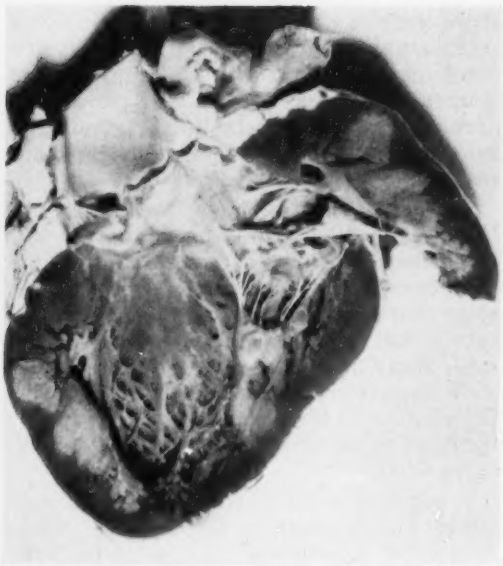

Fig. 4. Photograph of heart in case 3 exhibiting extensive gross involvement of the left ventricle by sarcoidosis.

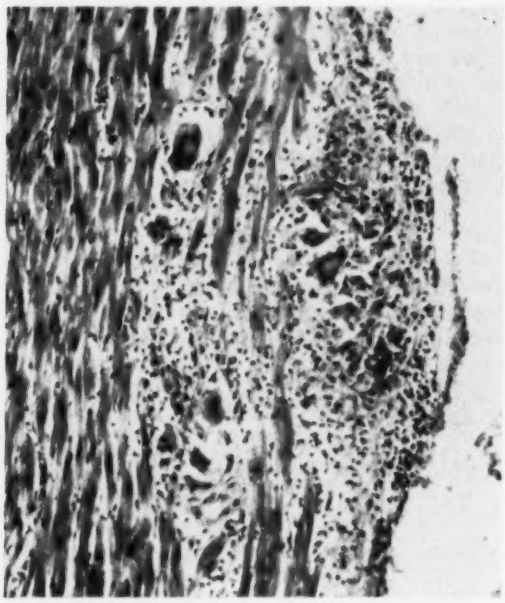

Fig. 5. Section of left ventricle in case 4, with a small sarcoid lesion involving myocardium and endocardium. (X 300).

lungs were tubercles composed of epithelioid cells and occasional giant cells. These tubercles showed no caseation. The hilar lymph nodes showed some scarring, with many scattered sarcoid tubercles. There were several epithelioid tubercles in the spleen and a few in the portal areas of the liver. Special stains on this material failed to reveal the presence of any organisms.

Case 4

A 45 year old Negro woman entered the hospital March 13, 1939, complaining of shortness of breath of seven days' duration. Eight weeks before admission, she began to have a cough with some sputum. She had some fever and was in bed for about two weeks. She had had a chronic cough until about seven days before admission, when she began to notice attacks of dyspnea, coughing, and wheezing. The temperature was 38 C., pulse 120, respiration 24, and blood pressure 145 systolic, 95 diastolic. The patient had a dry hacking cough. The sedimentation rate was 34 mm. per hour. Sputum examination was repeatedly negative for acid-fast organisms and fungi. Repeated skin tests with old tuberculin revealed a negative response down to 1 to 1000. Skin tests with numerous fungus antigens were also negative. Because of her asthmatic attacks she was treated with aminophylline and other drugs. Roentgenograms of the chest at several intervals revealed at first a diffuse soft nodular infiltration of the lower part of the left lung and the medial portion of the right lung. However, the process became more extensive and spread along the bronchi in a nodular pattern suggestive of a rapidly growing tumor. The electrocardiogram indicated auricular tachycardia but no evidence of myocardial disease. The hemogram was normal. The patient expired about two months after admission.

At autopsy the lungs showed small raised nodules a few millimeters in diameter on the pleural surfaces and scattered through the lung parenchyma. These were thought to be miliary granulomas. The heart showed no gross lesion. The liver exhibited small white nodules similar to those seen in the lungs. Similar nodules were seen in the spleen. The lymph nodes in the region of the mediastinum were enlarged.

On microscopic examination numerous sarcoid tubercles were seen scattered throughout the lungs, in the liver, spleen, and mediastinal lymph nodes. A few scattered tubercles were seen in the thyroid, the trachea, the myocardium, and the aorta. Special stains on this material failed to reveal the presence of any organisms. No caseous necrosis was found in the lesions, and the reticulum stains showed preservation of the reticulum in the centers of the lesions.

Comment

These 4 cases well illustrate the wide variation in the severity and distribution of myocardial lesions in sarcoid.

Case 1 exhibited sarcoid granulomas diffusely involving the auricular myocardium without affecting the ventricles at all (see figs. 1 and 2). However, other structures contiguous to the auricles — namely, the pericardium and superior vena cava—were involved. In the lungs were numerous sarcoid granulomas associated with fibrosis. This factor, along with the presence of essential hypertension, made interpretation of the clinical findings relative to the sarcoid lesions in the heart difficult.

Case 2 showed an extensive patchy fibrosis of the ventricular myocardium which in some areas extended from the epicardium to the endocardium, replacing much of the myocardial tissue. The areas of fibrosis con-

tained scattered irregular tubercles with a few round cells and occasional giant cells (fig. 3). The electrocardiogram was consistent with myocardial damage, and this patient died in congestive heart failure.

A similar case of myocardial sarcoid with the development of congestive heart failure was reported by Johnson and Jason[4]. The heart in their case showed extensive sarcoid lesions in the ventricles with some scarring. There was also a mural thrombus at the apex of the left ventricle. The electrocardiographic changes consisted of transient ventricular tachycardia, premature ventricular beats from multiple foci, and prolonged P-R intervals. Other cases terminating in congestive heart failure were reported by Ricker and Clark[5] and by Yesner and Silver[2].

Case 3 is an example of relatively sudden death due to myocardial sarcoidosis. This patient suddenly began to have palpitation and epigastric pain a few days before death. The electrocardiogram showed ventricular tachycardia, rate 180, and was interpreted as consistent with myocardial disease. The patient died suddenly 10 hours after admission.

At autopsy the heart showed a diffuse granulomatous process marked by epithelioid tubercles involving the left ventricle with destruction of muscle fibers (fig. 4). The endocardium was involved, but not the epicardium. Similar cases of sudden death have been reported by Scotti and McKeown[6], Kulka[7], Bates and Walsh[8], and Longcope and Fisher[9]. Most of these cases showed extensive myocardial sarcoidosis. Also, most of the cases with death due to heart lesions have occurred in Negroes[2], including the cases in the present series.

Case 4 showed only a few scattered epithelioid tubercles in the myocardium and endocardium (fig. 5). They were not responsible for any symptoms. Other cases showing incidental myocardial lesions in sarcoidosis were reported by Nickerson[10], and Skavlem and Ritterhoff[11].

Naturally, there have been attempts to associate specific clinical signs and symptoms with myocardial sarcoidosis. Bates and Walsh[8] suggested that unexplained tachycardia in known cases of Boeck's sarcoid pointed to the presence of myocardial involvement. However, other observers have pointed out that this change is not constant[2]. Two of the present cases (3 and 4) exhibited tachycardia, but in one (case 4) there were only minimal myocardial lesions, while another with extensive heart involvement (case 2) showed normal sinus rhythm. Yesner and Silver[2] stated that paroxysmal arrhythmia and defects in the conduction system are the most common clinical manifestations of myocardial sarcoid.

Longcope and Freiman[3] were impressed by the association of uveo-parotid fever with extensive myocardial sarcoidosis in the few fatal cases of this syndrome on record. They suggested that uveo-parotid fever may indicate a widely disseminated and active disease. Many of the cases in the literature do show an uveitis or a parotitis or both, but the association is not a constant one. None of the cases in the present series showed uveitis or parotitis.

It has been noted that 6 cases with skeletal muscle lesions reaching autopsy also showed myocardial sarcoidosis[12]. One of the present cases is included in that series. The reverse situation, however, has not held true. Only one of the present 4 cases of myocardial sarcoid showed skeletal muscle lesions. The cases of myocardial sarcoidosis, both in the literature and in this series, also showed lesions in the lungs, lymph nodes, liver, and spleen, these being the most common sites of sarcoid lesions[3]. Apparently the heart is the fifth most frequently involved organ, at least in the autopsy material[3].

Summary

Four new cases of myocardial sarcoidosis are reported, 2 of which ended fatally as a result of the myocardial lesions. The clinical and autopsy findings are discussed.

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HOW SAFE IS SPINAL ANESTHESIA IN PRESENT DAY PRACTICE?

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Within recent years doubt has been cast in certain circles concerning the feasibility of administering spinal subarachnoid block for the relief of pain during operations. Increasing numbers of reports stressing particularly neurologic complications have appeared[1]. One author has concluded: "From a neurological point of view, we give the opinion that spinal anesthesia should be rigidly reserved for those patients unable to accept a local or general anesthetic."[2]

Growing resistance towards this method of analgesia also is evident in the lay population. It is not unusual for a patient to refuse a spinal block because of personal knowledge of a friend who can date a persistent backache, paresthesia, or area of numbness from the administration of a spinal anesthetic.

From a statistical viewpoint, there is some indication, based on a series of 857,000 cases, that the mortality rate associated with spinal anesthesia is less than that accompanying general anesthesia[3]. It is impossible from the literature, however, to ascertain the incidence of neurologic sequelae following subarachnoid block. The distressing feature which emphasizes their occurrence is that the patient often lives, but in a physically incapacitated manner.

Numerous theories have been propounded and suggestions made to explain the etiologic factors involved in the production of spinal anesthetic morbidity and mortality. The answers are unknown in many instances. Yet certain clues may be found, some of which are related to the technical administration of the drug, some of which are concerned with the drug itself, and others which are allied with the care of the patient while analgesia exists. By following certain practices and taking adequate precautions, many potential pitfalls can be avoided, and the incidence of complications reduced.

Read before the Section on Anesthesia, Medical Society of the State of North Carolina, Pinehurst, May 12, 1953.

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Technical Administration

Before intrathecal injection is contemplated, it should be determined by history and examination whether the patient has had or is suffering from a neurologic disease. A spinal anesthetic may be associated with a recrudescence of previous symptoms. Medicolegal proceedings have been initiated linking paresthesias following spinal anesthesia to poliomyelitis which occurred 20 years previously[1a].

If a patient does not wish to have a spinal anesthetic, his request should be heeded whether his reasons be truly valid or not. It may be because of a sixth sense, but the patient often proves to be right. In the majority of situations, pain relief can be obtained by other methods.

Performance of lumbar puncture and injection of anesthetic solutions is fraught with danger, unless what may appear to some as elaborate preparations are made. Many authorities believe that the etiologic factors responsible for undesirable sequelae have their inception during the technical administration of the drug. It is almost a *sine qua non* that syringes, needles, and instruments employed for the spinal anesthsia should be autoclaved as a unit package. However, care must be taken even before this. A recent report [1d] describes neurologic sequelae developing from a detergent in which syringes were washed prior to autoclaving.

During the actual administration, aseptic precautions are just as necessary as for a surgical incision. Preferably the physician should scrub his hands and forearms before putting on gloves. The antiseptic which is used to cleanse the patient's back should be allowed to dry or be wiped off before the lumbar puncture needle is introduced. Chemical arachnoiditis can occur from the inadvertent introduction into the spinal canal of cleansing solutions[4].

Placing the patient in the proper position is necessary if the possibility of trauma is to be minimized. A one-shot tap is so much easier if every effort is made to have the vertebral column in a straight line with the spines separated as far as possible. Multiple attempts to find the subarachnoid space may

cause definite physical trauma, and certainly precipitate psychologic trauma.

The use of fine atraumatic needles is felt to lessen the possibility of postspinal headache. The exact cause of this vexing complication is unknown, but majority opinion adheres to the so-called leakage theory. This supposes that escape of cerebrospinal fluid from the hole in the dura made by the needle is sufficient to cause stretching of the cerebral vessels and associated headache. There is some indication that the employment of 24 to 26 gauge needles for the puncture reduces the incidence of this complication. The use of these small-bore needles, however, increases the technical difficulty of lumbar puncture.

From time to time when the subarachnoid space is entered, the patient will complain of pain or paresthesia at the site of puncture and radiating down the leg. This is probably caused by the needle impinging upon a nerve root. The position of the needle should be changed before the anesthetic solution is injected, as permanent neurologic sequelae have been reported to follow injection into a nerve root within the canal[5].

Everyone who performs lumbar punctures is familiar with the "bloody tap." The source of the bleeding is not always known, but frequently it is due to perforation of the venous plexus, which lies between the anterior part of the dura and the body of the vertebra. Withdrawal of the needle a few millimeters will produce clearing of the spinal fluid usually, and the anesthetic solution may then be injected. If the bloody fluid fails to clear, it is better to discontinue the procedure. Injection of a local anesthetic into a blood vessel can precipitate severe cardiovascular collapse or cerebral convulsions.

In order to prevent anesthetic failures, efforts should be made to insure that all the anesthetic solution is deposited within the subarachnoid space. Those with most experience feel that technical difficulties account for 99 per cent of the failures. It is rare to find a patient who is rachi-resistant. If spinal fluid can be withdrawn freely both before and after injection, it is moderately certain that the anesthetic has been deposited properly.

Anesthetic Drugs

Drugs for subarachnoid injection are supplied in ampules and are prepared either in solution or in crystalline forms. To prevent contamination, it is common practice to soak the ampules in an antiseptic solution prior to use. It is recognized that virtually all sterilizing solutions are capable of producing neurologic damage should they inadvertently be injected into the spinal canal. This is possible if an ampule is cracked and seepage occurs into it while it is being soaked. It is suspected that nerve damage has occurred in this manner. It has been shown[4] that alcohol, chlorophenyl, Bard-Parker solution, and mercurochrome are the worst offenders in this regard, while Zepharin and phenol are less likely to cause permanent damage. Coloring the sterilizing solution with a dye such as methylene blue will aid in detecting ampule contamination[6], but even with this help the naked eye may not detect the seepage[4]. Using only drugs which are prepared in crystalline form, particularly the niphinoid type, is a considerable protection, as fluid contamination is seen readily. The best way of circumventing this hazard entirely is to have all ampules autoclaved with the spinal tray or as a separate package.

The inherent toxicity of spinal anesthetic drugs to nerve tissue has been blamed in patients suffering neurologic sequelae. It is felt that the drugs in common usage are free from such effects, providing they are not injected in too high concentrations. For example, procaine in concentrations up to 5 per cent is considered safe, but a 10 per cent solution is capable of producing permanent nerve damage. All other factors considered equal, the more dilute the injected solution, the less likelihood of direct nerve involvement[7].

It is difficult to conceive of generalized toxic manifestations occurring from overdosage of the drug used for spinal anesthesia. However, true sensitivity can occur[8], although the incidence of this complication has been estimated to be as low as 1 in 200,000[9]. Such reactions usually appear as generalized convulsive movements beginning within 20 minutes after the injection. They can be controlled by the intravenous administration of a barbiturate and the inhalation of oxygen.

Care of the Patient

Backache is one of the most common complaints following spinal anesthesia. This may be due to localized trauma at the site of injection, but more probably results from the complete relaxation of the back muscles.

These muscles usually protect the ligaments of the back and pelvis against undue stretching and help to preserve the normal lordosis. Under spinal anesthesia this protection is lost, and abnormal strain upon structures not used to it may produce backache in the postoperative period. Placing a small pillow under the back to preserve the lordotic curve and another one under the knees to reduce the ligamentous pull may prevent this complication.

Of maximum importance following spinal injection is the preservation of normal respiratory and cardiovascular physiology. The level of analgesia must be high enough for the surgical procedure, but careful observation must be maintained to see that in this accomplishment there is no respiratory embarrassment or interference with cardiovascular dynamics. This requires the undivided attention of someone who is trained to detect untoward events. It is impossible to predict with any degree of accuracy what level of analgesia may be attained in any given patient with a given drug dosage administered by a given technique. Each patient presents a separate, individualized problem.

If the level of sensory analgesia rises higher than the seventh thoracic segment (level of xiphoid), it is likely that some degree of intercostal paralysis will be present. When the level is to the nipple line (fourth thoracic segment) or higher, respiratory ventilation definitely is diminished. With these conditions, however, the patient may have no complaints, and it will be difficult to notice any objective changes in his respiratory excursions. Such moderate involvement of the respiratory system should not be allowed to remain untreated. Over a period of time, in an insidious manner, chronic anoxia may develop and lead to an acute cardiorespiratory collapse. Adequate arterial oxygen saturation usually can be maintained by administering oxygen to the patient at a rate of 5 to 7 liters per minute by means of nasopharyngeal catheter. It is sound practice to administer oxygen in this way whenever the sensory level rises above the xiphoid, and in all patients over 60 years of age.

An acute emergency exists if the spinal level becomes so high that the patient complains of shortness of breath, becomes restless, and is unable to talk. Objectively his chest fails to expand during inspiration and he begins using his accessory muscles of respiration. Treatment here consists of giving oxygen to the patient by a face-mask from an anesthetic gas machine or oxygen tank and assisting the patient's attempts to breathe by manually compressing the rebreathing bag in synchrony with his efforts. This procedure may be lifesaving.

Table 1

Vasopressors

Agent	Dose (mg.) I. V.	Dose (mg.) I. M. or S. C.
Ephedrine	10-25	50
Methedrine	3-5	10-20
Vasoxyl	3-5	10-20
Neosynephrine	1-3	3-5

Levophed—continuous drip only—4 mg to 1000 cc.
Vasoxyl—continuous drip—20 mg. to 1000 cc.

As the level of analgesia ascends in the subarachnoid space, interference with vascular dynamics may complicate the picture of respiratory inefficiency. Paralysis of the sympathetic nervous system becomes more extensive as the anesthetic rises, with a critical point being reached at the level of the sixth to the fourth thoracic segments. If the systolic blood pressure falls more than one third of the preoperative reading, efforts should be made to correct it. At times cardiovascular collapse may occur within minutes of the injection and at an extremely rapid rate[10]. Cardiac arrest may ensue and require heroic resuscitative measures.

Hypotension following a spinal anesthesia may be prevented by injecting subcutaneously, prior to the lumbar puncture, a vasopressor such as ephedrine, 50 mg. This is a useful routine measure and is not contraindicated in the older age group. When blood pressure falls after administration, one of several vasopressors may be given (table 1). The anesthetist should use one with which he is familiar. Small doses may be given intravenously and larger doses intramuscularly. If preferred, a continuous intravenous drip of a dilute solution may be started. If cardiac arrest occurs suddenly, cardiac massage should be instituted within three minutes in order to prevent permanent cerebral damage.

The instant availability of oxygen, which can be administered under positive pressure, and a cannulated vein will assist immeasurably in preventing catastrophies under spinal anesthesia. The anesthetist will handicap himself and the patient if he does not have

Table 2

Sedation

Drug	Dose (Intravenous)*
Morphine	5 mg.
Demerol	25 mg.
Seconal	50 mg.
Nembutal	50 mg.

*Administer every 3 to 5 minutes until drowsy.

a gas machine and an open vein at his command.

The significance of fear or apprehension on the part of the patient under spinal is difficult to assess. Certainly it is an important consideration, since it is quite possible that a patient can be "scared to death." When preoperative medication has not provided sufficient sedation to overcome dread, one should not hestitate to administer narcotic or hypnotic drugs intravenously until the patient becomes drowsy (table 2). If the situation warrants, light general anesthesia may be preferable. Restlessness during the course of operation can result from anoxia, however, and this possibility should be ruled out before sedation is given.

Nausea or vomiting which occurs in the operating room usually is due to one of two causes. Frequently it accompanies the development of hypotension and actually may be instrumental in raising the blood pressure. At other times it is thought to be a reflex reaction precipitated by traction on the mesentery and transmitted through the splanchnic nerves. If the level of analgesia is to the fourth thoracic segment, this reflex action is seldom seen. Taking deep breaths or administering oxygen is an aid in overcoming this complication. If the blood pressure is low, vasopressors are indicated.

In patients suffering from acute intestinal obstruction, vomiting may occur as silent regurgitation. It is important to detect this immediately, as aspiration into the lungs can have fatal results.

Summary

An attempt has been made to discuss some of the factors which lead to trouble in spinal anesthesia. This is a technique which requires thoughtful preparation and execution. The responsibility of the administrator only begins with the injection of the drug. It ends in the recovery period when function of the nervous system is returning. Providing meticulous care is taken and common sense is exercised, analgesia by this method is considered to be as safe as by any other anesthesia technique. It should be reserved for patients who have no objection to it, for surgeons who desire it, and for anesthetists who can perform and supervise it carefully and intelligently.

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Discussion

Dr. David A. Davis (Chapel Hill): Dr. Stephen has brought up two or three points which I think deserve further emphasis.

The first of these concerns the sterilization of drugs used for spinal anesthesia. Not many of us realize that these drugs can be autoclaved. This is about the best way I know of insuring the sterility of these agents, either in solution or in the crystalline form.

The second point of emphasis is that spinal anesthesia should not be used on patients who refuse it, since in doing so the physician runs a great risk of incurring a malpractice suit. There are already on record, I am told, cases in which judgment has been rendered against a physician for performing spinal anesthesia against the patient's wishes. In one case "lumbar block" or some other term was substituted for "spinal anesthesia" in discussing the matter with the patient. The physician was sued and judgment rendered against him on the grounds of assault and battery for carrying out a procedure against the patient's wishes.

The third point is that many patients who would be classified as a fair or good risk for operation are very poor candidates for spinal anesthesia—for example, the obese patient, the patient with intestinal obstruction and distension, and the pregnant patient at term. I do not want to leave the impression that none of these patients should receive spinal anesthesia. Many of them can be managed successfully if certain things are remembered. The technique must be modified, however, in the presence of abdominal distension from whatever cause.

Dr. Richard Spencer (Greensboro): This is a most timely subject. Since Foster Kennedy's paper first appeared, I have found it more and more difficult to talk a patient into having a spinal anesthetic. Actually, I find it difficult even to suggest a spinal in Greensboro. The more the subject is discussed, both pro and con, the harder it is to give this type of anesthesia to a patient. I think this is because lay people are becoming acquainted with the controversy rather than with the facts in the case. They know that physicians disagree with regard to spinal anesthesia, and they have a natural dread of anything about which there is a doubt.

As to the techniques of administering spinal anesthesia, I wonder about the efficacy of injecting a vasopressor subcutaneously immediately before the spinal anesthetic is given. I say this because so often the spinal anesthetic is administered within a matter of 30 or 45 seconds from the time the vasopressor is given subcutaneously. In my opinion, that does not allow enough time for the vasopressor to be picked up by the general circulation, and by the time it has, hypotension may already have set in.

Dr. Archibald McIntosh (Marion): May I ask Dr. Stephen two questions? What would be his method of choice in the case of diabetic or arteriosclerotic gangrene? If it should be spinal and the patient refuses, then what would he use?

Dr. Sword (Asheville): One of the surgeons at Post-Graduate in New York made what to me was a very germane remark when he said, "When the magnitude of anesthesia is greater than the surgery to be performed, then I see no reason for doing a spinal."

There are times when I have been faced with two or three cases at once, and, as a matter of expediency, I have used spinals when I perhaps would not have done so otherwise. I don't think there is any excuse for doing a spinal for economic reasons.

I would like also to suggest that anybody who attempts a spinal anesthetic should be competent in handling the airway. Occasionally, serious respiratory difficulties follow spinals, and if the surgeon or the anesthetist is not competent to handle the airway, the laryngoscope, the bronchoscope, and so forth, he ought not to be doing a spinal.

Dr. C. R. Stephen (closing): I would like to thank the discussants for their comment.

We all have differences of opinion. The reason we think a vasopressor by hypodermic injection is of value at times is that if the blood pressure is going to fall following the administration of a spinal anesthetic, it will usually reach its lowest point in about 15 or 20 seconds. This is about the time one would expect a hypodermic injection to have its maximum effect.

With relation to the anesthetic for diabetic gangrene and associated arteriosclerosis, if the difficulty were in a lower extremity, we would use a so-called unilateral spinal anesthetic, in which we attempt to confine the anesthesia to one of the extremities by posturing at the time the drug is administered. That is probably as efficacious a way as any in which to provide this patient with pain relief.

If the patient refuses to have a spinal anesthetic, there are probably a number of different combinations of drugs, or variations of techniques which could be used. I think, personally, we probably would favor cyclopropane in such a patient, as we have a fair idea that we could maintain good oxygenation with that drug. It does not interfere too much with the metabolism or with the cardiovascular dynamics.

EARLY NORTH CAROLINA MEDICINE

NATIVE AND IMPORTED MEDICINES IN EIGHTEENTH CENTURY NORTH CAROLINA

DOROTHY LONG*

CHAPEL HILL

Letters, official reports, and advertisements referring both to native drugs and to medicines imported into the colony contribute to our picture of the practice of medicine in eighteenth century North Carolina. Among the earliest items is a report, dated May 21, 1707, from Robert Holden to the Lords of Trade. In describing North Carolina, "which I have been in and lived some time there," he said that it produced "for drugs rabbex serpentarius; saxafrax calamus, aramaticus assarebecca capillus ventris polypodium quercus, etc."[1] Shortly after this John Lawson, in his *New Voyage to North Carolina*, published a brief list of the native plants, and some years later Dr. John Brickell, who had practiced in North Carolina[2], gave a more detailed and scientific description of them in his *Natural History of North Carolina*, published in Dublin in 1737.

A number of individuals were interested in medical botany, but the Moravians, under the leadership of their first physician, Dr. Hans Martin Kalberlahn, were among the first groups in the state to make an effort to produce drugs. In 1756 a medicinal garden was laid out for Dr. Kalberlahn, and the following year the Moravian Records reported that he arranged a laboratory. Clewell's *History of Wachovia in North Carolina* contains a reproduction of the plan of this garden and a list of the plants which were grown, including yarrow, chamomile, hyssop, fennel, rue, hoarhound, plantain, larkspur, and white poppy[3]. In 1761 the Bethabara diary recorded the making of a careful survey of the native herbs, with reference to their medicinal value, and the finding of several useful ones, including "squasweed for rheumatism, 'milkweed' for pleurisy, 'Indian physic' for preventing fevers, 'Robert Plantin' a valuable antidote, as is also 'Snake Root' and much 'Holly'."[4] There are several scattered references to "the snake root,

*Dorothy Long, Reference Librarian, Division of Health Affairs Library, North Carolina Memorial Hospital, Chapel Hill, North Carolina.

called Robert's Planting," being used for the bites of poisonous spiders. The following year, 1762, the diarist reported that "A botanist from Philadelphia stopped on his journey and inspected our medicinal garden and certain other places. He said the slope below our God's Acre was a great treasure house."[5]

An unsigned Moravian manuscript of 1764, bearing the title *Wachau or Dobb's Parish*[6], which is attributed to Christian Gottleib Reuter, the surveyor, contains a list of both native and imported plants in the Wachovia area, and notes their medical uses as far as the author was cognizant of them. For example, he wrote of sassafras, which was "much used in medicine to purify the blood"; calamus, which "was first brought here by the sainted Kalberlahn"; and night shade, which was "a proved remedy for old, open, scorbutic sores, or salt rheum." The writer also commented on the plants in the medical garden, listed "Things that at present are not in the Wachau," and recorded some premiums which had been offered to encourage the production of various items, including cochineal, scammony, and opium. Years later, at the beginning of the nineteenth century, the Medical Society of North Carolina again tried to stimulate the growing of medicinal substances by offering prizes to those who successfully produced opium, rhubarb, and caster oil[7].

Drugs were imported as well as home grown, and as soon as newspapers and magazines began to be published they furnished a medium for advertisements. In 1764 the *North Carolina Magazine*, published in New Bern by James Davis, contained a notice by Robert Williams, offering for sale "the following medicines, fresh and new, from the original warehouse and true preparers in London, *viz.* James's fever powder Lockyer's pills, Turlington's balsam, Bateman's drops, Hooper's pills, Fraunce's elixir, Ratcliff's purging elixir, Anderson's pills, Godfrey's cordial, antimony, and flour of sulfur."[8]

In addition to such advertisements of proprietary medicines, there were other notices, often inserted by physicians, similar to the following items from the *North Carolina Gazette* of 1778.

> "The subscriber has for sale a quantity of medicines which are just imported, among which are the following articles, viz. Rheubarb, Jesuit's bark, glauber and epsom salts, tartar emetic, jallap, ipecacuanna, camphor, mercurius dulcis, corrosive sublimate, cantharides, sal nitre sulphur, crude salammoniac, myrrh, cinnamon, cloves, mace, etc. William Pasteur."[9]
>
> "I have just opened a large assortment of fresh imported medicines, among which there is a greater quantity of almost all the following articles than I could consume in my own practice in many years, therefore would be glad to supply others, at the lowest terms, with whatever they may want of Peruvian bark, camphire, sweet mercury, opium, rheubarb, jallap, ipecacuanha, aloes, myrrh, gummastick, magnesia, Spanish flies, Venice treacle, borax, saltpetre, volatile salt of hartshorn, do. of salamoniac, camomile flower, brimstone, and flowers of sulphur, &, &. Alex. Gaston."[10]

Dr. Gaston's advertisement appeared on May 22, 1778, and if he had a good supply of drugs at that time, it was an unusual circumstance, for from the beginning of the Revolution there had been complaints of the scarcity of medical supplies and instruments. The Journal of the Continental Congress, May 11, 1776, recorded an order that "Two sets of trepanning instruments and 100 lbs. of Peruvian bark be sent to North Carolina for the use of the continental troops in that colony."[11] A letter from Joseph Hewes to Samuel Johnston, written in Philadelphia a few days later, said that Congress had taken six North Carolina regiments into the Continental service and had ordered "Six chests of medicines and one hundred weight of bark for their use."[12] Ten days later he wrote again that "The wagon with the medicines will set off in two or three days; it waits only to have them properly put up, which takes some time. Those things that are most useful are beginning to grow scarce."[13] In December, 1776, the Provincial Council registered a complaint that a brigantine owned by Joseph Hewes and Robert Smith had been seized by a Massachusetts privateer, and listed Jesuit's bark as one of the valuable articles which it had contained[14].

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"The prime object of the medical profession is to render service to humanity; reward or financial gain is a subordinate consideration. Whoever chooses this profession assumes the obligation to conduct himself in accord with its ideals."—Principles of Medical Ethics of the American Medical Association, Chapter 1, Section 1.

JANUARY, 1954

MEAD JOHNSON AND COMPANY SETS A GOOD EXAMPLE

By a gift of chance, the December issue of the NORTH CAROLINA MEDICAL JOURNAL came in the same mail with the 1953 fall issue of "Mead Abstracts." A few of our readers may recall an editorial in the December issue of this journal, "The Postman's Burden," protesting against the huge volume of direct mail advertising that clutters doctors' desks and wastebaskets—more often the latter.

As if in reply, "Mead Abstracts" carried the following announcement:

With the fall issue, 1953 MEAD ABSTRACTS suspends publication.

In bringing you abstracted reports of significant developments and the latest authoritative thinking in the field of nutrition and related subjects, Mead Abstracts through the years has performed a unique service to the medical profession.

We feel that Mead Abstracts has well served its purpose and it is, therefore, with some reluctance that we suspend its publication.

Mead Johnson & Company is presently developing many new and better ways of serving the medical profession. One of these, for example, is our program of greatly increasing our scholarship award program for interns and residents.

We wish to reaffirm our dedication to the words which have guided our progress from the time of our Company's founding: "SERVAMUS FIDEM" . . . We Are Keeping the Faith.

Dr. Austin Smith, editor of the *Journal of the American Medical Association*, told the State Medical Journal Conference last November of a survey which had shown that for every dollar expended by pharmaceutical houses in direct mail advertising, a return of only $1.60 could be expected, whereas every dollar spent in medical journal advertising brought back $3.17. And if one may judge from the comments of doctors everywhere, the manufacturers may expect returns from direct advertising to diminish still more.

The NORTH CAROLINA MEDICAL JOURNAL congratulates Mead Johnson for doing its part to relieve the burden upon overworked doctors and their secretaries. May their worthy example be followed by many other manufacturers!

* * *

DR. EDWARD H. CARY

Dallas, Texas, lost one of its first citizens, American medicine lost one of its greatest leaders, and America lost one of her finest sons when Dr. Edward H. Cary died quietly at his home on December 10. He was active and useful to the very end of the almost 82 years of his life.

It is hard to overestimate the influence that Dr. Cary has had upon American medicine. Although he was born in Alabama and got his medical education in New York, he began practice in Dallas in 1901. That same year he was made dean of the University of Dallas Medical Department, later the Baylor University School of Medicine. He had a large part in the success of that school. After its removal to Houston in 1943, he founded and nursed to national recognition the South-

western Medical College. He also served as president of the Texas State Medical Association, of the Southern Medical Association, and of the American Medical Association. For many years he was chairman of the Legislative Committee of the A.M.A. He organized and was chairman of the National Physicians' Committee until, having accomplished its mission, it was disbanded after the American Medical Association employed Whitaker and Baxter to take over its public relations. It is not too much to say that he, more than any other one man, was responsible for checking the drive to possible federal control of medical practice in this country.

Few men could equal his ability to make and to hold friends. His personal magnetism, his genial manner, and his wise counsel endeared him to all sorts and conditions of men. His youthful spirit inspired many much younger than he to follow his leadership in medical groups. "Ed" Cary, as he was affectionately known by hundreds of friends, was a real medical statesman, whose influence will live for years to come. But how his friends will miss him!

* * *

CORTISONE AND ANTIBIOTICS

For some time it has been recognized that cortisone may have an unfavorable effect upon the course of certain infections. In order to protect the patient who is getting cortisone, antibiotics have been used. A pertinent question arose as to whether cortisone might impair the effectiveness of antibiotic agents. In an effort to obtain the answer to this question, Ernest Jawetz and Elizabeth R. Merrill of the University of California gave cortisone acetate to a test group of mice, who were then inoculated with *Klebsiella pneumoniae* and given Aureomycin or streptomycin in a varying dosage, "so adjusted as to cover a range from complete protection to none." A control group of mice was given the same treatment, except that no cortisone was administered. It was found that much larger doses of antibiotics were required to protect the mice who had had cortisone, whether Aureomycin or streptomycin was used.

"These experiments suggest that defenses of the host may materially aid the direct antimicrobial action of antibiotics. When cortisone depresses these host mechanisms, the manifest outcome appears to be an impairment of the therapeutic effect of the antibiotic."

The article strengthens the growing conviction that, while cortisone may be lifesaving in some conditions, it may be life-destroying in many infections.

1. Jawetz, Ernest, and Merrill, Elizabeth, R.: The Effect of Cortisone upon the Therapeutic Efficacy of Antibiotics, Science 118:549-550 (Nov. 6) 1953.

* * *

VICKSBURG DOCTORS BUILD GOOD PUBLIC RELATIONS

Dr. George Lull's Secretary's Letter for December 21 has a real human interest story of the recent terrible devastating tornado that did so much damage to Vicksburg, Mississippi:

The 40-odd doctors, members of the Issaquena-Sharkey-Warren Counties Medical Society, voted unanimously to give without charge all professional services rendered after the tragic storm.

Their action was all the more meaningful since the Mississippi legislature immediately voted $100,000 emergency relief, the National Guard expended about $75,000, President Eisenhower telephoned from Bermuda and authorized Civil Defense emergency funds, and the Red Cross turned up with funds and people.

Yet, the doctors of Vicksburg declined payment for services from private patients and several emergency funds.

After the storm struck, the doctors, with little or no rest, worked like Trojans to take care of the injured. Fortunately, the city's four hospitals, with a total bed capacity of slightly more than 400, were not damaged.

Since Vicksburg is a medical center, normal bed occupancy in these hospitals averages 75 per cent, or more than 300 patients. With about 250 injured persons requiring hospital treatment almost immediately following the storm, and in the face of tremendously adverse conditions, since both electric power and natural gas services were interrupted, the physicians and hospitals rendered outstanding and praiseworthy service.

It is to be hoped that this praiseworthy action will be as widely publicized as has been the unethical conduct of a few of our professional black sheep.

Committees and Organizations

ANESTHESIA STUDY COMMISSION

PREOPERATIVE PREPARATION OF THE PATIENT FOR ANESTHESIA AND SURGERY

LEONARD NANZETTA, M.D.

WINSTON-SALEM

Anesthesia, one of the greatest discoveries in medicine, remains nonetheless, a necessary evil: necessary, for the prevention of human suffering; evil, because its sometimes kills. Since the patient does not present himself for anesthesia *per se*, but rather for an operation under anesthesia, it behooves us to make anesthesia primarily safe, secondarily pleasant for the patient, and at the same time to provide ideal working conditions for the surgeon. In spite of the ever increasing demands made upon anesthesia by modern surgery, much of its danger and terror has been eliminated in recent years. Many of these deaths are preventable and can be attributed to failure to use intelligently knowledge that has been reaped from the seeds of over one hundred years of anesthetic experience. Of those deaths under anesthesia which are preventable, many are the result of mismanagement of the preoperative period.

Psychological Preparation

The first phase of preoperative preparation may be termed "psychological preparation." It begins at the moment when it is decided that an operation is to be performed. The patient's sudden realization that he has a pathologic condition which will require absence from his usual environment and interruption of his customary activities alarms him. Visions of multilation, dread of pain, and the possibility of death suddenly appear. Sympathy and reassurance by the family physician will do much toward allaying the patient's early apprehension.

Often the fear of anesthesia exceeds that of surgery. The attending physician can help much by assuring his patient that the safest form of anesthesia commensurate with the requirements of the surgery will be chosen. A patient's protest against a specific form of anesthesia should be respected. A few minutes spent in clarifying misconceptions, however, will often bring about acceptance of the anesthesia of the surgeon's and anesthetist's choice. Objection to spinal anesthesia is often based on the patient's fear of being awake while undergoing an operation. Assurance that pleasant sleep can be provided along with spinal anesthesia, often eliminates a great source of preoperative apprehension. Today it is seldom necessary to force a specific type of anesthesia on a patient.

Hospital personnel, hardened to hospital routine, must put themselves in the place of the patient. He is in unfamiliar surroundings in the midst of strange people, sights, sounds, and smells. He is subjected to all sorts of "clinical indignities." He is faced with one of the most disturbing of all fears—the fear of the unknown. Everything that can be done to make him comfortable and at ease will contribute in some measure to a smoother operative course and to his ultimate welfare.

Specific Preparation

The specific preparation for each patient will necessarily depend upon many factors. I will mention briefly only the most important. The nature of the operation, the age and physical status of the patient, the existence of complicating systemic disease, and the elective or emergency character of the operation must all be considered.

For elective surgery, admission to the hospital at least 24 hours before operation is mandatory. Time is needed to accomplish the necessary physical examination and laboratory work. A complete blood count and routine urinalysis should be done on each patient. Other laboratory and roentgen examinations are made as indicated and evaluated by the attending physician preoperatively. Anemia and abnormal fluid balance must be corrected by appropriate intravenous therapy. Heart disease should be appraised and treated. In an emergency or semi-emergency situation congestive heart failure can be treated by rapid digitalization, using one of the intravenous digitalis derivatives such as Cedilanid. Patients with cardiac decompensation are grave risks for anesthesia and surgery. They can usually be converted to relatively good risks rapidly by appropriate medical therapy.

Obviously many systemic conditions cannot be treated adequately in the minimum 24 hour preoperative period. One should not be tempted to "take a chance" with an elective operation when the patient is in less than his optimum condition medically. Minor

operations are frequent, but minor anesthesias are rare.

Before an anesthetic is given, the patient must have an empty stomach. Death from aspiration of stomach contents is probably the greatest single cause of death under anesthesia. Waters[1] writes: "For each patient who has died from postoperative pneumonia due to the irritation of his lungs with the vapors of ether, dozens have died . . following mechanical obstruction to their air passages. For each patient whose heart has stopped during anesthesia because of drug effect on the autonomic mechanism which controls it, the hearts of dozens of patients have stopped because the larynx was flooded with vomitus."

Patients who are scheduled for afternoon operations need not be starved. Strained fruit juice, a piece of dry toast, and coffee or tea with sugar may be given in the early morning. An empty stomach must be assured in those patients who enter for emergency surgery. Following trauma gastric emptying time is greatly delayed. Undigested food may be found in the stomach six to eight hours or longer after eating when the trauma supervenes before digestion is completed. The boy who falls from the cherry tree and breaks his arm in all likelihood has a stomach full of cherries many hours later. Only too often such a child is hurried to the hospital and given a general anesthetic for reduction of the fracture without consideration of the hazard his full stomach presents. The fact that the operation will be of short duration makes the anesthesia no less risky. Death from inhaling stomach contents during induction of anesthesia can and does occur. During prenatal visits obstetric patients must be told in emphatic terms not to eat after the earliest signs of labor become evident. Many women, early in labor, feel they must eat before going to the hospital in order to be fortified for the ordeal ahead. This practice has contributed to untold maternal deaths.

Premedication

Pre-anesthetic medication is an integral part of the anesthesia, and must be ordered carefully. It must not be reduced to a routine. An understanding of the purposes of premedication and a knowledge of the pharmacology of the drugs commonly used is essential for the rational administration of these drugs.

Pre-anesthetic medication has four principal functions: (1) the minimizing of fear and anxiety; (2) the reduction of metabolism; (3) the elevation of the pain threshold, and (4) the depression of certain undesirable effects produced by the anesthetic. Specific drugs are used for their actions in one or more of these categories.

Drugs used in premedication fall into three groups: (1) The barbiturates, used primarily for sleep or sedation; (2) the opiates, for decreasing metabolic activity, elevating the pain threshold, and diminishing fear; and (3) the belladonna derivatives, atropine and scopolamine, valuable for their action in depressing salivary secretions and noxious vagal reflexes. These drugs should be given with their specific functions in mind. They should be given at the optimum time and by the proper route to insure the desired peak effect at the time the patient goes to the operating room. The barbiturates, the opiates, and the belladonna derivatives used for premedication may all be given subcutaneously, intramuscularly, or intravenously with equal safety. Morphine given subcutaneously exerts its full effect in 90 minutes, intramuscularly in 45 minutes, and intravenously in 5 to 15 minutes, with some immediate effect when given by the latter route.

These drugs are given in the same dosage intravenously as when administered by the other routes. One sixth grain of morphine is dissolved in 5 cc. of saline and injected at the rate of 1 cc. per minute. This method offers the advantage that injection may be stopped when the desired effect is produced. It insures control over both excess and inadequate dosage. Cullen[2] writes:

"In anesthetic practice intravenous injection prevents the simultaneous development of the accumulative effect of the anesthetic drug and morphine depression at the termination of the anesthesia. Too many patients' lives are seriously endangered and lost through the following practice:

"Morphine is given subcutaneously a half hour or less prior to surgery. The anesthesia lasts approximately one hour, and at its conclusion the patient has the maximal effect of both the anesthetic agent and the morphine. He is returned to the ward or room with respiratory depression; obstruction develops, followed by asphyxia, and he dies. Had the morphine been given in a manner which permitted the development of its total action before induction of the anesthesia, its effect would be wearing off during the anesthesia and there would be minimal combined depression at the conclusion of the anesthesia."

The morphine substitutes Pantopon, Dilaudid, methadone, Demerol, and Dromoran may all be given by the intravenous route in the same manner as morphine.

Summary

A brief review of some of the factors in pre-anesthetic and preoperative preparation is presented. Psychological preparation, adequate physical examination, preoperative correction of certain pathologic states, and pre-anesthetic medication are discussed. The danger associated with a full stomach preoperatively is emphasized.

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AMERICAN COLLEGE OF CHEST PHYSICIANS

Report of the Joint Committee on Chest X-Ray

Purpose of Joint Committee on Diseases of the Chest

In establishing a Joint Committee on Diseases of the Chest, the purpose of the American College of Chest Physicians and the American College of Radiology is to exchange ideas and to propose guiding principles on the problems involved in routine chest x-rays in hospitals (general, mental, etc.), and mass chest x-ray programs. The committee agrees: that each physician should be encouraged to have a chest x-ray of all of his patients; that every patient admitted to a hospital, private or public, should have a routine chest x-ray; and that the follow-up for all suspected lesions seen in chest x-ray surveys should be organized very carefully to assure that the patient comes under medical supervision.

Limits of Survey

Routine chest x-ray examinations should be defined as those examinations of the chest which are conducted to screen persons with abnormal changes of the chest from persons with normal chests. The examinations are screening diagnostic procedures and are not to be considered as clinical diagnostic examinations. The screening method is for the purpose of detecting the presence or absence of a lesion only.

The size of the film which one uses for screening purposes is not of primary importance. The committee believes in principle, however, that when microfilms have been used, a 14 x 17 inch film is a necessary second step in the screening procedure and the mechanism whereby such is provided in any community shall be determined by the local medical society or the local hospital staff. Survey chest x-rays either in hospitals or in the general population are approved as a screening device if conducted by agencies which utilize well qualified professional and technical personnel and which make sincere efforts to send the positive individuals to qualified local physicians or clinics for proper follow-up.

Interpretation and Report

Interpretation and reporting of medical findings is a medical matter and should bear the signature or identification of the responsible physician.

Method of Reporting

Method of reporting of chest survey studies: This is a local matter and is by prearranged agreement between the employer and the employee in industrial surveys; in other surveys it is in accord with medical ethics, according to local agreement.

Type of Reporting

Type of reporting: The Committee discourages the reporting of suspicious cases as tuberculosis. It believes this to be a clinical diagnosis. The x-ray interpreter should designate the cases that require immediate follow-up as "urgent." The small film x-ray interpretation is merely an impression.

It should be emphasized that the 14 x 17 inch film is a diagnostic aid and the results derived therefrom are also impressions and not diagnoses. Even the larger film is but one of several examinations necessary in order to establish correct diagnoses.

Double Reading

The committee notes the several publications indicating the extent of false negative and false positive reports resulting from inter- and intra-individual variations in interpretations of chest films. From these it is evident that failures to detect tuberculosis can be reduced by multiple readings, but at the expense of increasing the false positives, unless a check mechanism is employed. The simplest elaboration of multiple reading is the independent interpretation of the film by two physicians with referee conference of the two undertaken in those cases in which they disagree. Only those cases on which both agree in conference should be followed.

While such a procedure may result in the detection of a slightly larger portion of all the abnormal cases, it may not be feasible from an economic or personnel standpoint. Groups responsible for survey operations are urged by the committee to give consideration to double reading as one of the methods by which survey yields may be increased. Availability of financial resources and qualified professional personnel, as well as the need for other services of relative importance, will be determinates in this decision. The committee, therefore, calls attention to some of the virtues of double reading but does not recommend it unreservedly.

Professional Compensation

The professional cost of performing routine chest examinations in hospitals: The Joint Committee believes the radiologist and/or chest physician should be compensated just as any other physician practicing his profession. The procedure is time consuming and places a definite responsibility on the radiologist or chest physician. The Committee likewise felt that in this matter the basic principle of payment is by arrangement between the physician and the hospital or agency involved. In the reading of follow-up films there should also be an individual limit to the number of films which should be read in any one day by one physician and which he should not exceed. The compensation, of course, would have to take into consideration, whether the physician makes the film in addition to interpreting it.

Clothing of Patients

Whether or not a screening examination can be conducted with the patient fully clothed: Since the number of lesions overlooked because of clothing (2 per cent) is considerably smaller than the normal variations of interpretation (Chamberlin, etc.) have demonstrated to exist in the reading of photofluorographic films, it is concluded that the examination of clothed persons is as effective a procedure as examination of the undressed persons. Since examination of the fully clothed persons is an easier procedure as compared with the examination of the undressed persons, the Committee agreed that screening examination may be conducted with the patient fully clothed.

Approved by Joint Committee on Chest X-ray: American College of Radiology, American College of Chest Physicians, February 4, 1953.

Reprinted from Diseases of the Chest 28:589 (May) 1953.

Reader's Qualifications

Qualifications of readers in mass chest surveys: It was believed at the present time there was no practical method which could be used to evaluate the qualifications of a particular reader. Studies in this respect are being made at the present time. It is hoped that within a short period of time satisfactory testing methods will be available. The committee therefore agreed to leave this matter open for further discussion.

Protection

The radiation received by all professional, technical and clerical personnel associated with photofluorographic equipment should be continuously monitored by means of film badges or other devices which have been proved to be satisfactory for determining the radiation exposure of personnel.

When an individual receives more than 100 milliroentgens per week, the medical officer in charge of the unit should immediately determine whether the individual has been careless or whether the protective devices of the equipment are at fault.

If the fault lies with the individual, the individual should be informed of the fact and strongly cautioned regarding the dangers of excessive radiation exposure. Failure to regard such warning should be considered as negligence on the part of the individual.

If the fault lies with the equipment or protective devices, the photofluorographic unit should immediately be taken out of commission until such time that measurements of radiation conditions where technical or clerical personnel are required to work will yield radiation exposures less than 100 milliroentgens per week for case loads of 2,500 exposures at 95 kv. and 40 ma. seconds (the average exposure per photofluorographic chest film).

Continuation of Study

It is recommended that the Joint Committee arrangement continue and that the Joint Committee meet annually, or at the call of the co-chairmen. In an effort to have the Joint Committee act continuously and without interruption, interim ideas should be sent to the co-chairmen, and an exchange of opinion should continue during the intervals between meetings. Recommendations are solicited from all interested in the affairs of the Joint Committee.

* * *

Joint Committee on Chest X-Ray

American College of Radiology: Leo G. Rigler, Minneapolis, Minnesota, Chairman; Sydney J. Hawley, Seattle, Washington; Russell H. Morgan, Baltimore, Maryland; E. P. Pendergrass, Philadelphia, Pennsylvania; Paul C. Swenson, Philadelphia, Pennsylvania.

American College of Chest Physicians: Otto L. Bettag, Chicago, Illinois, Chairman; Robert J. Anderson, Washington, D. C.; Hollis E. Johnson, Nashville, Tennessee; Edward Kupka, Berkeley, California; James H. Stygall, Indianapolis, Indiana.

Winthrop Names Dr. Sayers to Medical Research Staff

Dr. Ross V. Sayers has been appointed assistant director of medical research for Winthrop-Stearns Inc., pharmaceutical manufacturer, it was announced by Dr. Theodore G. Klumpp, president.

Dr. Sayers will assist Dr. J. B. Rice, director, and Dr. A. Scribner, associate director, in arranging for clinical testing of Winthrop's drug products prior, and subsequent, to their introduction to doctors and the drug trade.

CORRESPONDENCE

To the Editor:

Is there any known disease besides malaria that causes headaches, usually of rather severe intensity and often of lifelong duration, in which administration of most any of the antimalaria drugs brings prompt and lasting relief of the headache?

Over a period of ten years I have treated several hundred cases that would classify under the above description. I make thick and thin blood smears, stain with Giemsa stain from Gradwohl in St. Louis, and thus am able to identify objects which I think are malaria parasites; which are either greatly thinned out or disappear entirely as the headaches vanish on administration of antimalaria drugs. However, my efforts to find a laboratory which will agree with my findings are not successful. Our North Carolina State laboratory and other public health authorities say the chromatin in these objects is not red enough or the blue of them blue enough for them to be malaria parasites.

Any help you can render in regard to my problem will be appreciated and may be the means of relieving many headaches in the South.

JOHN H. KENDALL, M.D.
Clinton, North Carolina

(The foregoing letter was submitted to a competent pathologist, whose answer follows.—Ed.)

The late Dr. Fred Hanes approached questionable instances of malaria with the maxim that if one was in doubt, the patient did not have malaria. In the cases mentioned here it would seem doubtful that such a large focus of malaria would exist alone and, further, without producing identifiable parasites in blood smears. Since so many artefacts may resemble malaria parasites to the untutored eye anxious to find them, it would be well to accept the word of the public health authorities mentioned that they are not present in the smears.

The matter of the "lifelong duration" of the headaches is not so easy, and is really beyond the scope of this question. It is assumed that lifelong means adult life. Probably the most common cause of such headaches is "tension," that vague force resulting from the accumulated impact of life on the individual. That such headaches are re-

lievable by a vast variety of agents is a matter of common medical knowledge. The *post hoc* evidence of their disappearance following antimalaria therapy proves nothing about their relationship to malaria. Careful and exhaustive controls are necessary, and, as Stewart Wolff has shown, even placebos are not without activity in the form of the circumstances under which they are given. In an experimental situation such as the one at hand, no valid conclusions are justified.

To the Editor:

Enclosed is a copy of the invocation given by Joseph H. Carter, D.D., minister of the First Presbyterian Church of Newton, North Carolina, at the Ninth District Medical Meeting in Newton on September 24, 1953.

Several of the members commented upon the fitness of the invocation and have requested that I ask Dr. Carter to allow it to be sent to the JOURNAL for publication, if desired.

F. W. JONES, M.D.
Past President
Ninth District Medical Society

* * *

INVOCATION

JOSEPH H. CARTER, D.D.

NEWTON

As we sense the majesty and the mystery of the ETERNAL, we would be reverent and humble. We would be grateful for the gift of thinking—and what a thrill! And what a sweep! From the germ to the galaxies and constellations, and what a study! This intriguing study of Divine artistry revealed in the frame and function of these temples in which we live.

We would be grateful for the urge to "find out and to help out" that has inspired men and women down through the centuries to devote their time and their talent to the ministry of health and healing, and for the grand resultants that today are helping to win the war against the killers of men.

As we stand in the line of one of the world's great traditions of skill and service, we would here and now re-dedicate our lives to faithful, honest, sympathetic and unmeasured service to those who need us and our service so desperately, those who have the right to our very best, and those whose very lives are woven into the fabric of friendship with and dependence upon our own.

And most of all we would pray for a true sense of life's values as we represent a profession that gives us so much and of us expects so much more.

In the name of the Great Physician, Amen.

BULLETIN BOARD

COMING MEETINGS

North Carolina Academy of General Practice Postgraduate Seminar—Winston-Salem, January 24.

North Carolina Sectional Meeting, American College of Surgeons—Charlotte, February 1-2.

Public Relations Conference, Medical Society of the State of North Carolina—Sir Walter Hotel, Raleigh, February 12.

Southeastern Division Regional Meeting, United States Section of the International College of Surgeons—West Palm Beach, Florida, January 29-30.

Louise Obici Memorial Hospital Clinical Conference—Suffolk, Virginia, February 10.

American College of Chest Physicians, Second Regional Postgraduate Course on Diseases of the Chest—New Orleans, Louisiana, February 15-19.

Fourteenth Annual Congress on Industrial Health—Louisville, Kentucky, February 23-25.

National Conference on Rural Health — Dallas, Texas, March 4-6.

New Orleans Graduate Medical Assembly—New Orleans, Louisiana, March 8-11.

Southeastern Surgical Congress — Birmingham, Alabama, March 8-11.

NEWS NOTES FROM THE DUKE UNIVERSITY SCHOOL OF MEDICINE

Dr. Ewald W. Busse, chairman of the Department of Psychiatry, has just been elected a fellow in the American College of Physicians.

Dr. Busse took over duties as director of Duke's Psychiatry Department, November 1, coming here from Colorado General Hospital, where he served as chief of the Division of Psychosomatic Medicine. He also served as director of the electroencephalograph laboratory, Colorado Psychopathic Hospital. He is carrying out research studies in physiologic changes in schizophrenic patients, mental health in elderly people, and methods of teaching psychosomatic concepts to students.

Other Duke doctors who are fellows in the American College of Physicians are J. Lamar Callaway, W. C. Davison, Macdonald Dick, Oscar Hansen-Pruss, James P. Hendrix, Walter Kempner, Elijah E. Menefee, William N. Nicholson, Edward S. Orgain, E. L. Persons, ACP governor for North Carolina, Julian M. Ruffin, R. Wayne Rundles, David T. Smith, and Eugene A. Stead.

Those who are associates are Drs. George Baylin, Frank Engel, John Hickam, Samuel P. Martin, John Pfeiffer, Theodore Schwartz, James V. Warren, and E. Charles Kunkle.

NORTH CAROLINA SOCIETY FOR CRIPPLED CHILDREN AND ADULTS

Since 1947, when the Society for Crippled Children was instrumental in the passage of the Special Education Act in North Carolina, $22,383.64 has been contributed to the special education programs over the state, according to information just released by Albin Pikutis, executive director. This

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WRITE TODAY

amount was spent as one of the statewide projects of the Society. The biggest part of this expenditure has been in the form of grants to the institutions of higher learning for workshops and teacher-training programs.

The University of North Carolina, until 1950, was the only institution in the state offering any training for teachers in the field of special education. In 1950 a grant was made to East Carolina College in Greenville to conduct a summer workshop for teachers in special education.

In 1951 North Carolina State College in Raleigh, West Carolina College in Cullowhee, and North Carolina College in Durham, added special education to their summer curriculum, and since that time have been increasing this program steadily in order to help train more teachers in this field.

The need for special education teachers in the state still exceeds the number of persons available who are trained in this field—but the picture looks brighter each year—thanks in part to your EASTER SEAL contributions.

Iredell-Alexander Counties Medical Society

At the annual meeting the Iredell-Alexander Counties Medical Society held in Statesville on December 8, 1953, the following officers were elected for 1954: president—Dr. John T. Stegall, Statesville; vice president—Dr. L. B. MacBrayer, III, Mooresville; secretary-treasurer, Dr. Ernest Ward, Statesville.

The following physicians were elected to membership in the society: Drs. P. L. Munday, J. H. Nicholson, II, Frank S. Parrott, and Harry S. Allen, Jr., all of Statesville.

Delegates are as follows: Drs. J. S. Holbrook, Statesville; George H. Givens, Jr., Taylorsville; W. W. Painter, Mooresville. Alternate Delegates are: Drs. J. L. Pressly, H. F. Long Hospital, Statesville; A. S. Moffett, Taylorsville; L. B. MacBrayer, III, Mooresville.

Dr. J. B. Aycock, Stearns Building, Statesville, has been notified of his certification as a Diplomate of the American Board of Radiology.

Durham-Orange County Medical Society

The Durham-Orange County Medical Society held its annual Christmas party at the Hope Valley Country Club in Durham on Wednesday night, December 9. Following a social hour, dinner was served to 316 members and their wives, husbands, and guests. Lucky numbers were drawn for gifts. The group was entertained by Wallace the Magician. Dancing followed.

The only business transacted was the election of officers and new members. Dr. T. T. Jones of Durham was elected president; Dr. Leonard Fields of Chapel Hill was elected vice president; and Dr. William Shingleton of Duke University was elected secretary-treasurer. Elected to the executive committee was Dr. K. M. Brinkhous of the University of North Carolina. Dr. Guy L. Odom of Duke was elected to the Board of Censors. Delegates to the North Carolina Medical Society are Drs. Larry Turner, John Glasson, and William T. Sealy.

The electees will take office at the first meeting following the State Medical Society Meeting in May.

Edgecombe-Nash Medical Society

The monthly meeting of the Edgecombe-Nash Medical Society held in Rocky Mount on December 9 was largely devoted to the election of officers. In addition, the members heard a brief talk on medical management.

Forsyth County Medical Society

Speaker for the December meeting of the Forsyth County Medical Society was Dr. Ivan W. Brown, Jr., assistant professor of surgery at Duke University, whose subject was "Problems in Blood Transfusion Therapy."

News Notes

Dr. James A. Valone, formerly associated with Dr. James Barrett Brown of St. Louis, has opened his office for the practice of plastic and reconstructive surgery at Cameron Village, 2107 Clark Avenue, Raleigh.

* * *

Dr. Alexander Sweel has announced the opening of his office for the practice of psychiatry at 1950 West First Street, Winston-Salem.

* * *

Dr. George W. James of Winston-Salem announces the removal of his offices to 207 South Hawthorne Road on February 1, for the practice of dermatology and syphilology.

* * *

Dr. Porter F. Crawford has announced the opening of his office for the practice of dermatology at 272 North Graham-Hopedale Road, Burlington.

Louise Obici Memorial Hospital Clinical Conference

The second annual Clinical Conference of the Louise Obici Memorial Hospital at Suffolk, Virginia, will be held on February 10. The following program has been announced.

MORNING SESSION

Dr. W. Holmes Chapman, Presiding

10:15 to 11:00 Dr. Charles C. Congdon, "Total-body Irradiation in Man and Laboratory Animals: Experimental Therapy"

11:00 to 11:45 Dr. John P. Collins, "Fluid Balance in the Surgical Patient"

11:45 Recess

12 Noon to 12:45 Dr. R. Cannon Eley, "Vomiting in Infancy and Childhood"

AFTERNOON SESSION

Dr. Lawrence J. Stetson, Presiding

2:15 to 3:00 Lt. Col. Joseph L. Bernier, "The Diagnosis and Management of Oral Tumors"

3:00 to 4:00 Dr. Harry F. Dowling, "Current Changes in Antibiotic Therapy"

4:15 to 5:00 Dr. Harry Walker, Clinical Pathological Conference

EVENING SESSION

6:00 Cocktail Party—Courtesy of Tri-County Medical Society

7:00 to 9:00 DINNER
(Speaker)
Dr. Thomas C. Fleming, "Drug Therapy in Hypertension"

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Radiological Society of North America

Dr. J. Rush Shull of Charlotte was elected vice president of the Radiological Society of North America at its annual convention held at the Palmer House in Chicago, December 13-18.

Dr. Shull has been North Carolina counselor for the organization for 12 years. Other new officers are: Dr. Eugene P. Pendergrass of the University of Pennsylvania; Philadelphia, president, and Dr. Thomas B. Bond of Fort Worth, Texas, president-elect. The next convention will be held at the Biltmore Hotel in Los Angeles next December.

New Orleans Graduate Medical Assembly

The seventeenth annual meeting of the New Orleans Graduate Medical Assembly will be held March 8-11. The registration fee of $20 includes lectures, three-dimensional motion pictures, clinics, symposiums, clinicopathologic conferences, technical exhibits, three round-table luncheons, and many other features.

The continued heavy demand for hotel accomodations in New Orleans makes it imperative that physicians who plan to attend the assembly write without delay for reservations. Requests for reservations should be addressed to Chairman, Hotel Reservations Committee, The New Orleans Graduate Medical Assembly, Box 1460, New Orleans 5, Louisiana. Since hotel reservations can be made only for registered attendants of the Assembly, the registration fee should be sent at the same time to The New Orleans Graduate Medical Assembly, 1430 Tulane Avenue, New Orleans 12, Louisiana.

Attendance at the assembly provides acceptable medical study requirements for continued membership in the American Academy of General Practice.

Southeastern Surgical Congress

The Southeastern Surgical Congress, will hold its twenty-second annual meeting in Birmingham at the Dinkler-Tutwiler Hotel, March 8-11. Panel discussion on traumatic lesions, esophagogastrointestinal hemorrhage, liver and gallbladder pathology, and surgical management of peptic ulcer will be held in addition to individual papers by an imposing roster of speakers.

International College of Surgeons

Southeastern Division Regional Meeting

The Southeastern Division regional meeting of the United States Section of the International College of Surgeons will be held at West Palm Beach, Florida, on January 29 and 30, with headquarters at the Hotel Pennsylvania.

Dr. Lloyd J. Netto, 319 Clematis Street, West Palm Beach, Florida is in charge of the general arrangements and will furnish further information.

American College of Chest Physicians

The Council on Postgraduate Medical Education of the American College of Chest Physicians, in cooperation with the respective state chapters of the College as well as the staffs and faculties of the local hospitals and medical schools, will sponsor the second Regional Postgraduate Course on Diseases of the Chest in New Orleans, Louisiana, February 15-19, 1954, and the seventh annual Postgraduate Course on Diseases of the Chest to be held at the Bellevue-Stratford Hotel, Philadelphia, Pennsylvania, March 15-19, 1954.

These postgraduate courses endeavor to bring physicians up to date on recent advancements in the diagnosis and treatment of heart and lung disease. Tuition for each course is $75.

Further information may be secured by writing to the Executive Director, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

News Notes from the American Medical Association

Congress on Industrial Health

Ways of keeping well workers well and on the job are among the topics to be considered by representatives of labor, management and medicine at the fourteenth annual Congress on Industrial Health. Sponsored by the A.M.A.'s Council on Industrial Health, the Kentucky State Medical Association, and a number of additional national and regional groups interested in health and safety for the smaller industrial plant, the meeting will be held February 24-25 at the Brown Hotel, Louisville, Kentucky.

* * *

Miami Society Conducts Plaque Poll

Universal display of the A.M.A. plaque, "To All My Patients," in doctors' offices was recommended by the majority of the Miami, Florida, physicians responding to a recent informal poll conducted by the Dade County Medical Association. Many favorable comments on the plaque were received from physicians, whereas only one doctor gave a definitely unfavorable response.

To help practicing physicians create better relations with their patients, the American Medical Association is continuing to offer this plaque for one dollar, postpaid. Direct your requests for the plaque to the Order Department, American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois.

* * *

School Health Film Now Available

How a typical town in Oklahoma recognized its school health problems and, through community effort, launched a plan to solve them is the subject of a new film which has been added to the A.M.A. motion picture library. "School Health in Action"—a sound and color film—was produced for the Oklahoma State Department of Health with the cooperation of the Oklahoma State Medical Association. The service charge for this film is $2.00. Requests should be made to the A.M.A.'s Committee on Medical Motion Pictures.

* * *

Medical Education Meeting Set for February

Discussions of interest to medical schools and licensing boards will be aired at the fiftieth annual Congress on Medical Education and Licensure February 7-8-9 at the Palmer House, Chicago. Conducted under the auspices of the A.M.A.'s Council on Medical Education and Hospitals and the Federation of State Medical Boards of the United States, the Congress program will be built around a golden anniversary theme. More than 500 medical educators, officers and members of state licensing boards, and others interested in postgraduate medical education are expected to attend.

National Conference on Rural Health

The roles of community planning, cooperative efforts, nutrition, and insurance in the maintenance of healthful conditions in agricultural areas will be discussed at the ninth annual National Conference on Rural Health in Dallas, Texas, March 4-6.

The conference, sponsored by the American Medical Association's Council on Rrual Health, will be held in the Baker Hotel.

Dr. Edward J. McCormick, Toledo, Ohio, president of the American Medical Association, will be the speaker at the closing session. Also participating in that program will be Dr. Joseph I. Greenwell, New Haven, Kentucky, who at the Clinical Session of the A.M.A. in St. Louis last December was named as the "General Practitioner of the Year."

Dr. Carll S. Mundy, Toledo, acting chairman of the Council on Rural Health, speaking at the opening session, will sound the conference keynote — "Let's Put More 'U' in CommUNITY."

There will be panels on community programs, nutrition and health insurance. Principal presentations will be made by Mrs. Charlotte R. Bensen, Raleigh, North Carolina, health education consultant of the Medical Society of North Carolina; Dr. John B. Youmans, Nashville, dean of the Vanderbilt University School of Medicine and member of the A.M.A. Council on Foods and Nutrition, and Lambert Schultz, Chattanooga, staff executive of the group department, Provident Life and Accident Company. J. P. Schmidt, Columbus, Ohio, professor of rural sociology at the University of Ohio, will be the discussion leader for all three panels, each of which will have three other participants.

State committees on rural health will hold a preconference meeting with the A.M.A. Council on Rural Health on Thursday morning, March 4. The topics will include prepaid insurance and the physician's responsibility to his community.

Trudeau-Saranac Institute

Dr. Gerrit Willem Hendrik Schepers of Johannesburg, South Africa, has been named director of the Saranac Laboratory of the Trudeau-Saranac Institute, Trudeau, New York He is expected to assume his new duties in the late spring.

United States Atomic Energy Commission

Sixty-nine unclassified research contracts in the fields of biology and medicine were awarded by the U. S. Atomic Energy Commission during July, August and September, 1953. These contracts are awarded to universities and private institutions as a part of the AEC's continuing policy of assisting and fostering research and development in fields related to atomic energy as specified in the Atomic Energy Act of 1946.

Pan American Congress of Ophthalmology

Plans are well advanced for the Third Interim Congress of the Pan American Association of Ophthalmology, which is to be held in Sao Paulo, Brazil, June 17-21, 1954.

Dr. Moacyr E. Alvaro, Sao Paulo, president of the Association, has announced that the scientific sessions of the Congress will be devoted to presentation of recent advances in treatment of diseases of the eye and in the prevention of blindness.

NEUROPSYCHIATRIC JOURNALS INTEGRATED

The **Quarterly Review of Psychiatry and Neurology** will be integrated with the **Journal of Clinical and Experimental Psychopathology** commencing January, 1954. The new journal will continue to appear quarterly, and, although the number of pages will be almost double, the subscription price will remain at $11.00 a year.

The **Journal of Clinical and Experimental Psychopathology** and the **Quarterly Review of Psychiatry and Neurology** will include original articles written by outstanding authorities in the field of psychiatry, and abstracts which review current national and international psychiatric literature. All phases of psychiatric research and practice—biologic, chemical, psychologic, physiologic, and social will be covered.

Each journal will maintain separate editorial boards, with Dr. Winfred Overholser as editor of the **Quarterly Review of Psychiatry and Neurology**, and Dr. Arthur M. Sackler as editor of the **Journal of Clinical and Experimental Psychopathology**.

(BULLETIN BOARD CONTINUED ON PAGE 52)

AD CAMPAIGN SEEKS NEW MEMBERS FOR WORLD MEDICAL ASSOCIATION

The biggest advertising campaign yet designed to encourage American doctors to join the United States Committee of the increasingly important World Medical Association is under way with the participation of the leading medical advertising agencies.

The world group is devoted to the interests of freedom in medicine and to the exchange of new medical experience. It is also noted for extensive research projects and studies of the educational requirements everywhere.

Contributing to the campaign are: L. W. Frohlich and Company; William Douglas McAdams; Noyes and Sproul; Cortez Enloe; Paul Klempner; and Robert Wilson. These agencies formed a committee to work with the World Medical Association.

Layouts of the advertisements are being done at L. W. Frohlich. Copy is being prepared by Cortez Enloe. Medical journals are contributing space; for example, the **North Carolina Medical Journal** donated one page a month for four months.

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BOOK REVIEWS

Cure Your Nerves Yourself. By Louis E. Bisch, M.D., Ph.D. 247 pages. Price, $3.50. New York: Wilfred Funk, Inc., 1953.

In this book a very competent psychiatrist makes a commendable attempt to help the large number of people with poorly balanced nervous systems. The book is well written, sound, and at least is not calculated to frighten the reader. This reviewer, however, is inclined to agree with Campbell:

"While normal persons, and even some depressive patients, may obtain solace and satisfaction from reading certain books, the writer has reached the conclusion that the benefit to be expected from this form of therapy has been grossly exaggerated."(1)

The experience of this reviewer is that most people with chronic anxiety states or with mental depression will pick out from a whole chapter of such a book every sentence or phrase which is at all discouraging. For example, a sentence on page 68—"What we teach children sticks in their plastic minds and motivates them for life"—made one reader of this book more sure than ever that the pattern of her thinking had been irrevocably fixed and that there was no hope for improvement. The rest of the good advice in the chapter made little impression afterwards.

If, however, the doctor who does not have time nor inclination to talk with nervous patients wants to prescribe a self-help book, this one is about as good as anything that has appeared since John Rathbone Oliver's "Fear" was published many years ago. It is doubtful, however, if Osler's little classic, "A Way of Life," which is now more than a half-century old, will ever be improved upon as a means of helping people to overcome nervous tension.

1. Campbell, J. D.: Manic-Depressive Disease, Philadelphia, J. P. Lippincott, 1953, p. 338.

The Story of the General Adaptation Syndrome. By Hans Selye. 225 pages. Price, $4.50. Montreal, Canada: Acta, Incorporated, 1952.

The chronologic development of the "General Adaptation Syndrome" (G.A.S.) of Dr. Selye is related by him here in a series of seven "lectures" in a uniquely informal narrative style. These lectures were originally delivered to a heterogeneous audience of medical students, interns, residents, physicians and other medical personnel, and are not in a strictly objective style intended for research scientists. Thus the tenor of the whole book is highly personal. Dr. Selye does well in this style, for his similes are well drawn, his progressions are logical and easily followed, and the book is replete with his famous diagrams illustrating his ideas.

The tracing of his early concepts and logic based upon the facts concerning adaptation is very frank and at times even confessional in nature when he admits to some of the early claims for which he was so often criticized. This development of the concept of a pattern of adaptation in animals to nonspecific stress-producing agents is well handled, so that the reader is not apt to go further with theory than the facts permit. In the realm of those concepts relating to "diseases caused by derailment of adaptation," however, the incautious and inexperienced reader is more apt (in spite of the author's cautioning words) to gain the impression that the full explanation of many of our foremost diseases—arthritis, hypertension, nephritis, rheumatic fever, and so forth—in terms of hormonal imbalances is almost at hand.

This danger seems to be most evident after the

fifth lecture in which the progressive chronologic tracing of the various modifications of theories to fit new facts is brought up to date. In the following lecture, however, the author changes to a much more objective appraisal of the facts relating to adaptation which are considered as established, and belatedly illustrates with photographs the pathology of changes which he had been discussing beforehand. Possibly this concentration of illustrations is economically necessary.

The concluding lecture is a free-swinging discussion of the many criticisms that have been raised against various portions of the theory. Many of these criticisms which he lists and answers are obviously no longer valid in the light of present facts. All objections are handled quite conclusively, however; and, in addition, Dr. Selye raises and answers several of his own. As the author points out, perhaps the best defense of the theory is that, although there has been much criticism, no one has yet attempted to explain the process of adaptation by another theory.

As an introduction to the whole problem of stress for the uninitiated, this book is probably the best available at present. It is regrettable that the quality of the binding is extremely poor and became very frayed in one perusal. This should not detract, however, from a highly readable discourse on an extremely pertinent topic—namely, how do we meet the stresses of life.

Transactions of the American College of Cardiology. Volume 11 — 1952. Edited by Bruno Kisch, M.D. 252 pages. Price, $5.00. New York: American College of Cardiology, 1953.

A wide range of subjects of cardiovascular interest is covered in this volume. In general, the articles are concise and to the point. The accompanying bibliographies are probably the most useful feature of the book. The sections dealing with the rehabilitation of the cardiac patient are both pertinent and excellent.

This book will be of greatest value to the physician working principally in the field of cardiovascular disease.

Classified Advertisements

SPECIAL PHYSICIAN and FAMILY TOUR of Canadian Rockies, California, and Mexico in connection with A.M.A. San Francisco meeting in June. Twenty-Day SOUTHERN A.M.A. SPECIAL, 8,000 mile all expense tour. June 13 to July 2, 1954. HOTELS, BOATS, TRAINS, MOTOR TRIPS, Etc., all reserved before you start — $445. MOYERS TRAVEL BUREAU, 34-38 Peachtree Street, N. W., Atlanta, Ga. PLAN NOW — A REAL VACATION OPPORTUNITY.

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Raleigh, N. C.

In Memoriam

SAMUEL DACE McPHERSON, M.D.

Dr. S. D. McPherson, 80, of 29 Oak Drive, Durham, founder of McPherson Hospital and a nationally known medical leader, died at 2:35 a.m., September 12, 1953, at Watts Hospital, after a critical illness of one month.

Samuel Dace McPherson was born near Liberty, North Carolina, on April 20, 1873. He was the son of the late Samuel and Mrs. Martha Teague McPherson.

He received his primary education in the Liberty Academy. Later he attended the Medical School of the University of North Carolina, where he took his first two years of medicine, and transferred then to the University of Maryland Medical School, from which he graduated in 1903.

Following graduation, he entered the general practice of medicine in Haw River, North Carolina, and practiced there for eight years. But he was not satisfied with general practice, and in 1911 he entered the New York Polyclinic Institute, where for two years he took special training in diseases of the eye, ear, nose, and throat. He finished his training in 1913 and began practice in Durham, North Carolina, this time confining his work to eye, ear, nose, and throat.

In 1926 he built the McPherson Hospital, which he enlarged in 1937 and again in 1949. At the opening of the hospital, there were only two doctors on the staff. The number was gradually increased until some time before his death it reached seven.

Dr. McPherson was a past president of the Durham-Orange County Medical Society and the Durham Y. M. C. A. He was chairman of the Durham County Board of Health for more than 20 years. He was a member of the First Presbyterian Church, where he served as elder. He was a fellow of the American Academy of Ophthalmology and Otolaryngology, the American Medical Association, and the American College of Surgeons. He was a member of the Southern Medical Association and the Tri-State Medical Association.

The Durham-Orange County Medical Society, in a meeting at the Hope Valley Country Club on September 13, 1950, honored Dr. McPherson for his contribution to medicine. At the meeting the late Dr. William deB. MacNider discussed Dr. McPherson's medical accomplishments and his rise to prominence in national medical circles. The occasion was Dr. McPherson's retirement to consulting practice and hospital administration at McPherson Hospital.

Dr. McPherson's wife, the former Miss Katie Lee Banks, died in 1951. Survivors include one son, Dr. S. D. McPherson, Jr., of Durham, and one daughter, Mrs. F. G. Harper, Jr., of Hickory.

* * *

It was my privilege to know Samuel Dace McPherson for something more than 30 years.

He was not, in the strictest sense, a modern American in that he was not a seeker of security. On the contrary, he was a believer in opportunity, and he made those opportunities come true. He was an indefatigable worker, and he gave of himself unsparingly. I am sure that he never worked more than 24 hours in a day, but I am just as sure that he would have if there had been more hours. He loved people and he loved his work.

He did and said many things which, if they had been written down in the history of medicine, would be a great help to all future doctors. He made one statement to me which has helped me on many an occasion: "I have never seen a pain." I have never heard a young doctor or a nurse say, "I don't believe that this patient is having pain," without recalling this statement made by this man who had seen so many patients over so many years. It has made me give many a patient the benefit of the doubt, and I expect to continue to do so.

Dace McPherson was a great neighbor, a great friend, a great doctor and in the final analysis, a great man.

BULLETIN BOARD

(CONTINUED FROM PAGE 50)

CONGRESS OF INDUSTRIAL HEALTH

Health problems of the worker and his family will be discussed at the fourteenth annual Congress on Industrial Health, to be held February 23-25 at the Brown Hotel, Louisville, under sponsorship of the American Medical Association's Council on Industrial Health.

UNITED CEREBRAL PALSY

United Cerebral Palsy allotted research and training grants totaling $392,874 during the 12 months ending September 30, Leonard H. Goldenson, U.C.P. president and president of American Broadcasting-Paramount Theatres, Inc., announced in his annual report which has just been made public.

Mr. Goldenson stated that research grants totaled $254,940, a 69 per cent increase over the previous year. Speaking of the importance of research, Mr. Goldenson said: "The eventual conquest of cerebral palsy will come in the same manner that has proved successful with other health foes—through organized research. Only through research can we discover the basic causes, better methods or techniques of treatment, and above all, possible means of prevention."

DEPARTMENT OF THE ARMY

Posthumous award of the Army's Certificate of Achievement and the unveiling of a bronze plaque in honor of the late Col. Roy D. Halloran, MC, was held recently at the Walter Reed Army Medical Center, Washington, D. C.

VETERANS ADMINISTRATION

Veterans Administration is reviewing its records to determine whether certain living veterans or dependents of certain deceased veterans may be entitled to compensation for active nonpulmonary tuberculosis that developed within three years after separation from active service.

VA said the review is being conducted under Public Law 241, eighty-third Congress, enacted August 8, 1953. This law provides that if certain veterans develop active nonpulmonary tuberculosis to a compensable degree within three years from separation from active war-time service, it may be presumed to have been incurred in service providing there is no affirmative evidence to the contrary. The law also requires at least 90 days of active war-time service and a discharge or separation under other than dishonorable conditions.

Prior to the passage of this law, only pulmonary tuberculosis could be presumed to be service-connected for certain veterans if it developed within three years after separation from war-time service. The new law adds all other types of tuberculosis.

The Problem of Nausea and Vomiting:

ITS TREATMENT WITH DRAMAMINE®

Whenever nausea, vomiting and vertigo are disturbing and complicating factors, Dramamine may be used with confidence.

Keats[1] outlines the wide list of conditions in which Dramamine (brand of dimenhydrinate) has proved valuable as follows: "It has been well established in the control of motion sickness. It has been used effectively in the prevention and treatment of seasickness, airsickness, [in the treatment of] the nausea of pregnancy, Ménière's syndrome, . . . radiation sickness . . . and postfenestration reactions. . . . The site of action is imperfectly understood, but there is indication of an action of depressing labyrinthine function or its neural pathways, a highly selective central action, or both. Few side reactions of this drug have been noted."

The usual dose for motion sickness is 50 mg. (one tablet) taken one-half hour before departure and, if necessary, before meals for the duration of the journey. Control of nausea and vomiting of other conditions and severe motion sickness is achieved, with minimal drowsiness, by a dosage of 100 mg. every four hours.

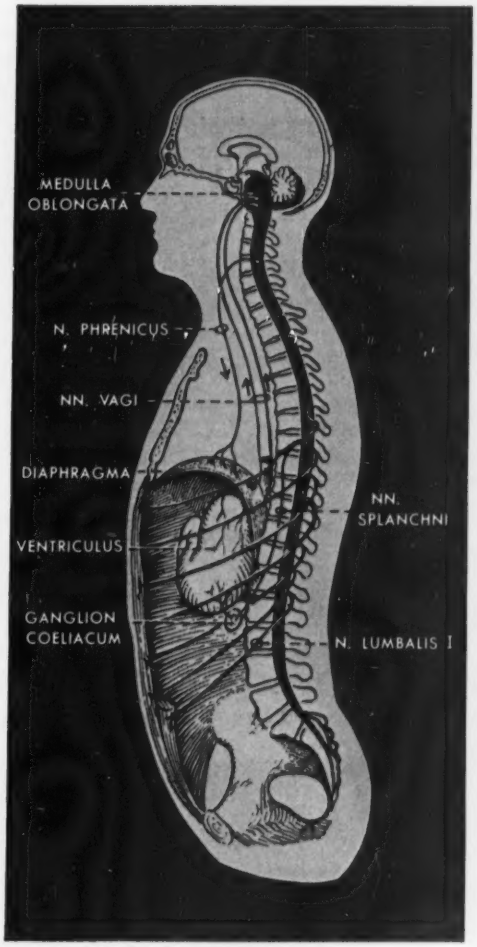
"[Dramamine] is administered orally or rectally. . . . The same doses may be administered rectally by insertion of the tablet or other suitable form. . . ."[2]

Dramamine Liquid is particularly useful for children.

Dramamine is accepted by the Council on Pharmacy and Chemistry of the American Medical Association.

1. Keats, S.: Ataxic Cerebral Palsy with Akinetic Seizures: Dramatic Response to Dramamine, J. M. Soc. New Jersey *50*:53 (Feb.) 1953.

2. Council on Pharmacy and Chemistry: New and Nonofficial Remedies, 1953, Philadelphia, J. B. Lippincott Company, 1953, p. 471.



THE VOMITING REFLEX: *Vagus → nodose ganglion → solitary tract → spinal cord → cervical, thoracic and lumbar nerves to diaphragm, cardiac sphincter, stomach, abdominal and pelvic musculature. (After Krieg, W. J. S.: Functional Neuroanatomy, ed. 2, New York, The Blakiston Company, Inc., 1953, p. 104.)*

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REFERENCES

1. Cathie, I.A.B., and MacFarlane, J.C.W.: Brit. M. J. 1:805 (April 11) 1953.
2. Coriell, L.L., and others: Antibiotics & Chemotherapy 3:357 (April) 1953.
3. Barach, A.L.: Geriatrics 8:423 (August) 1953
4. Finberg, L., Loventer, I., and Tramer, A.: Antibiotics & Chemotherapy 3:353 (April) 1953
5. Editorial: Antibiotics & Chemotherapy 3:347 (April) 1953.

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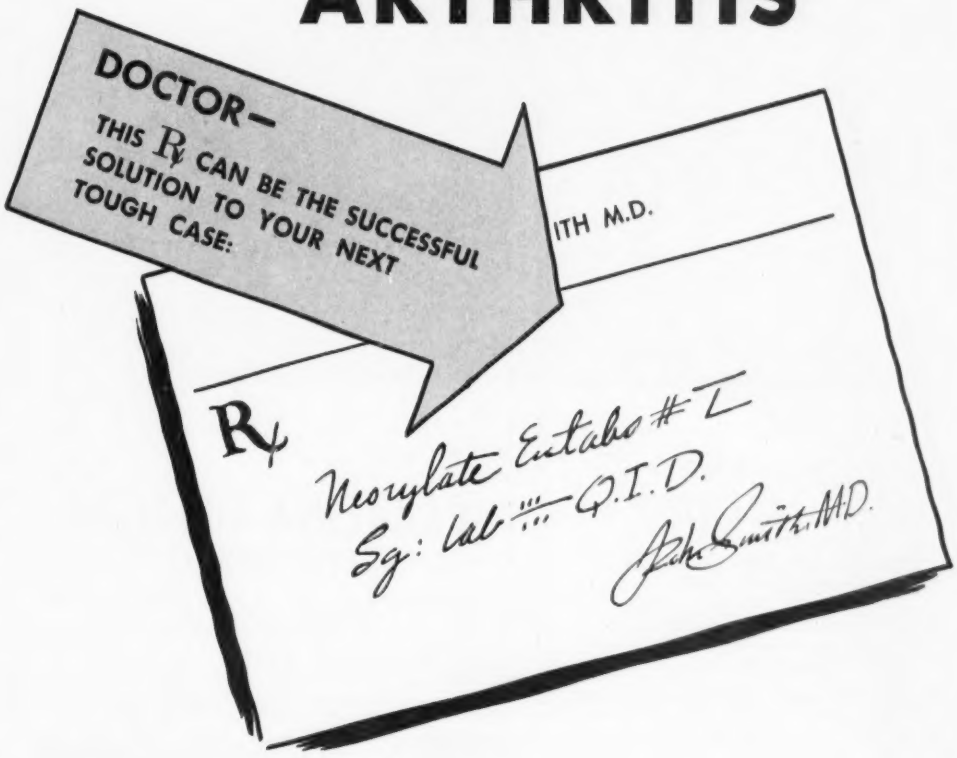

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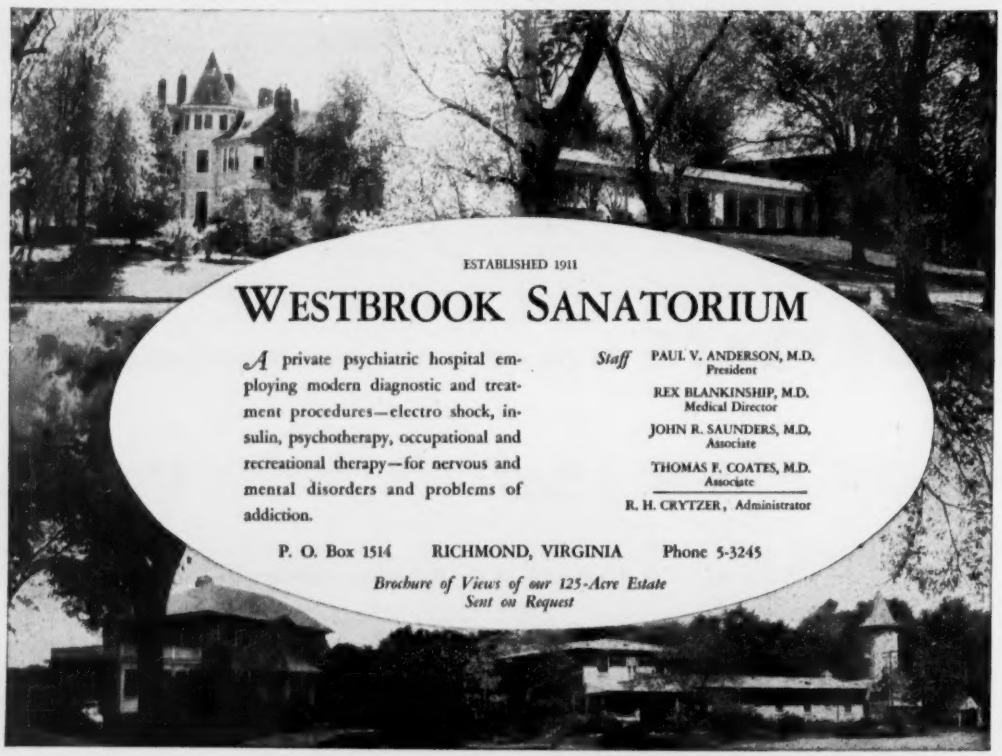
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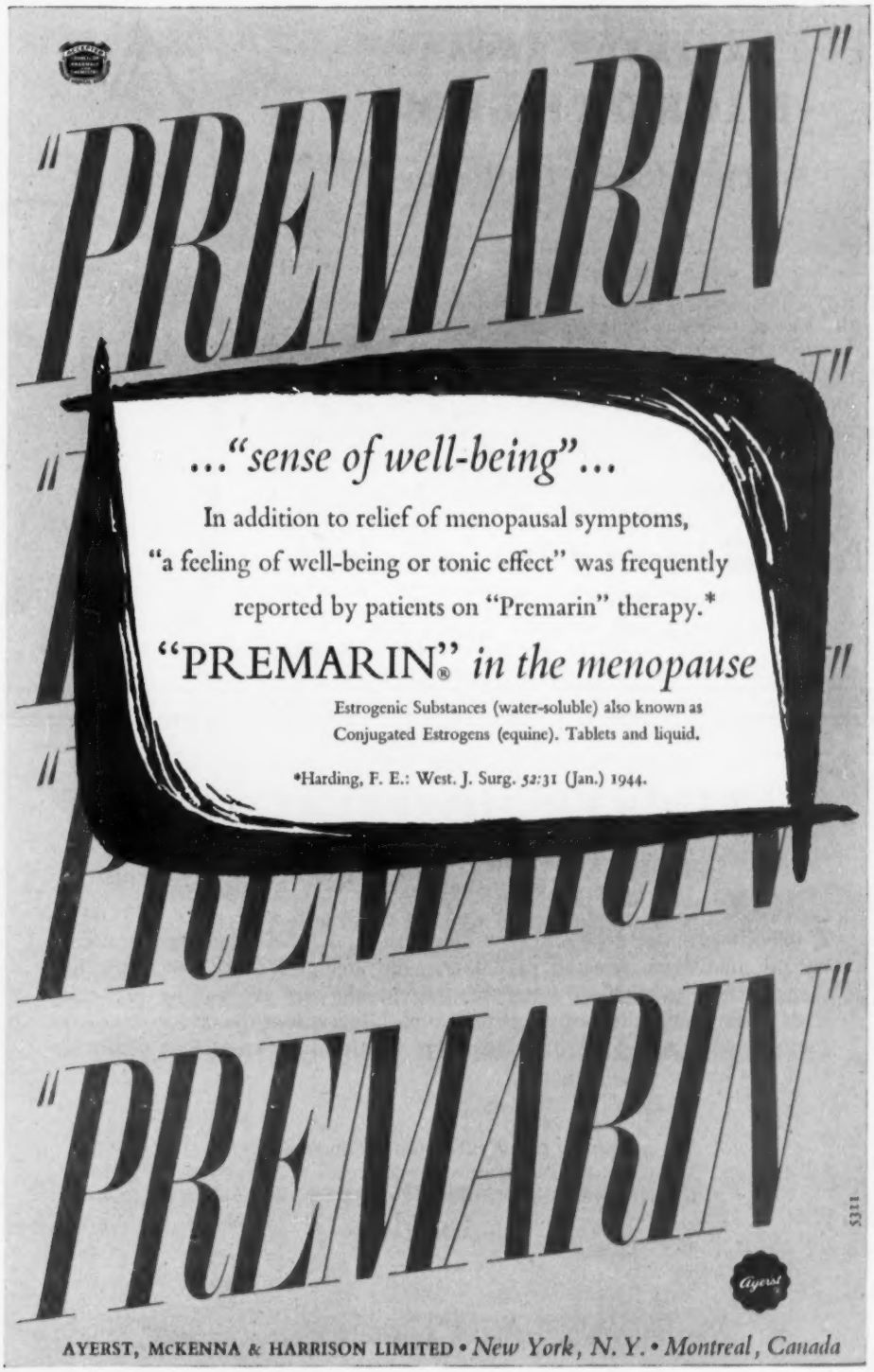
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•Harding, F. E.: West. J. Surg. 52:31 (Jan.) 1944.
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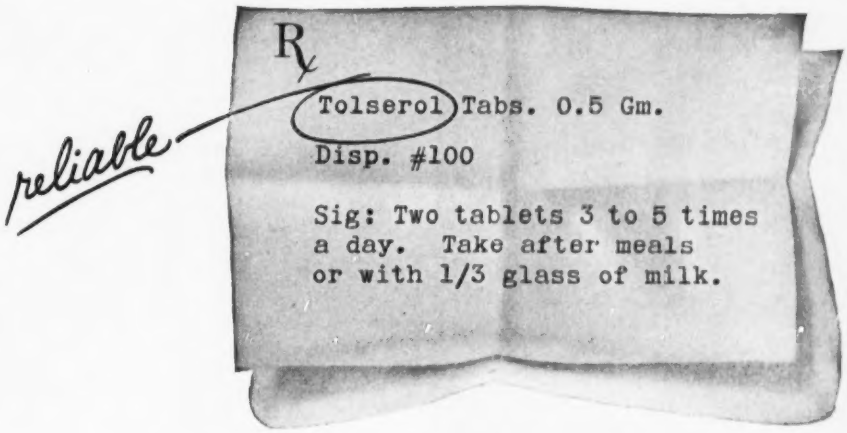

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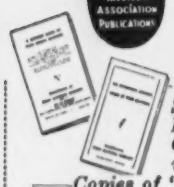

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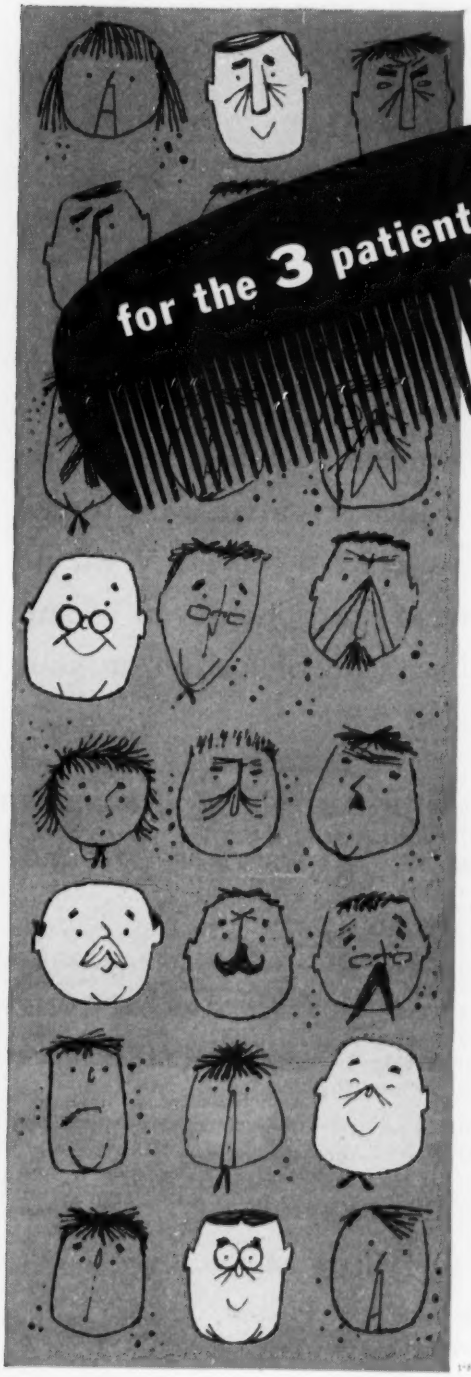

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1. Slepyan, A. H. (1952), Arch. Dermat. & Syph., 65:228, February. 2. Slinger, W. N. and Hubbard, D. M. (1951), *ibid.*, 64:41, July. 3. Sauer, G. C. (1952), J. Missouri M. A., 49:911, November.

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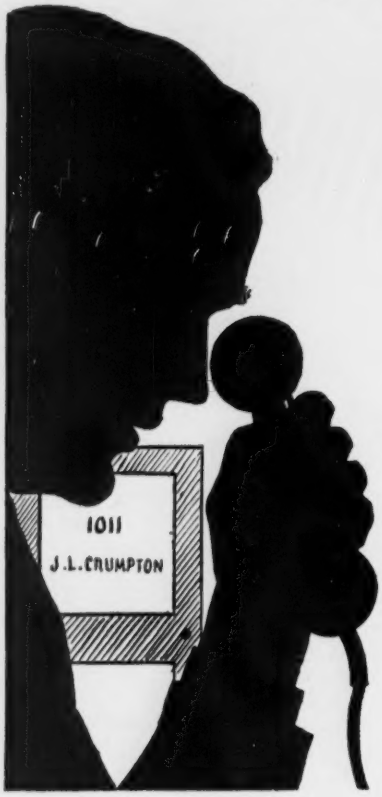

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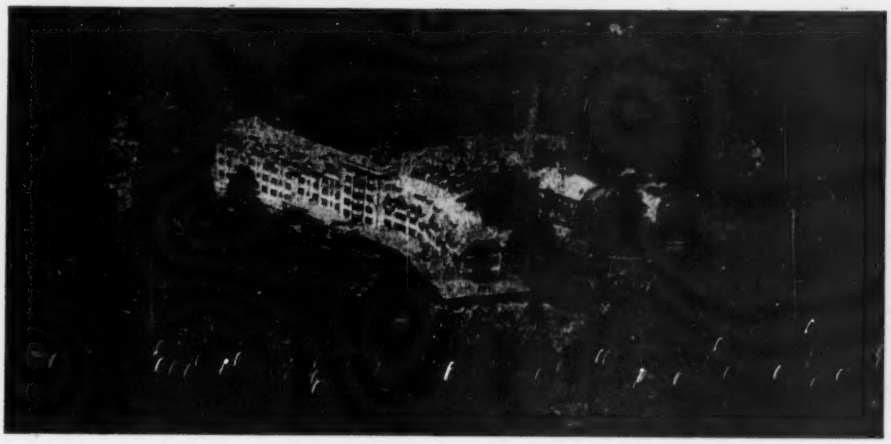

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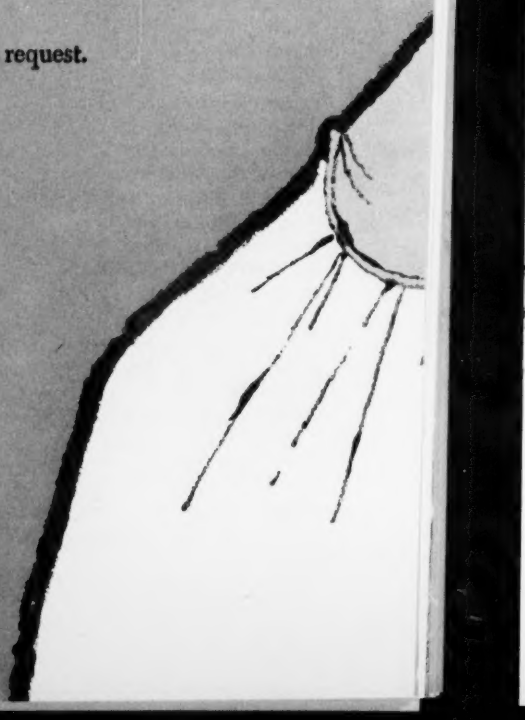

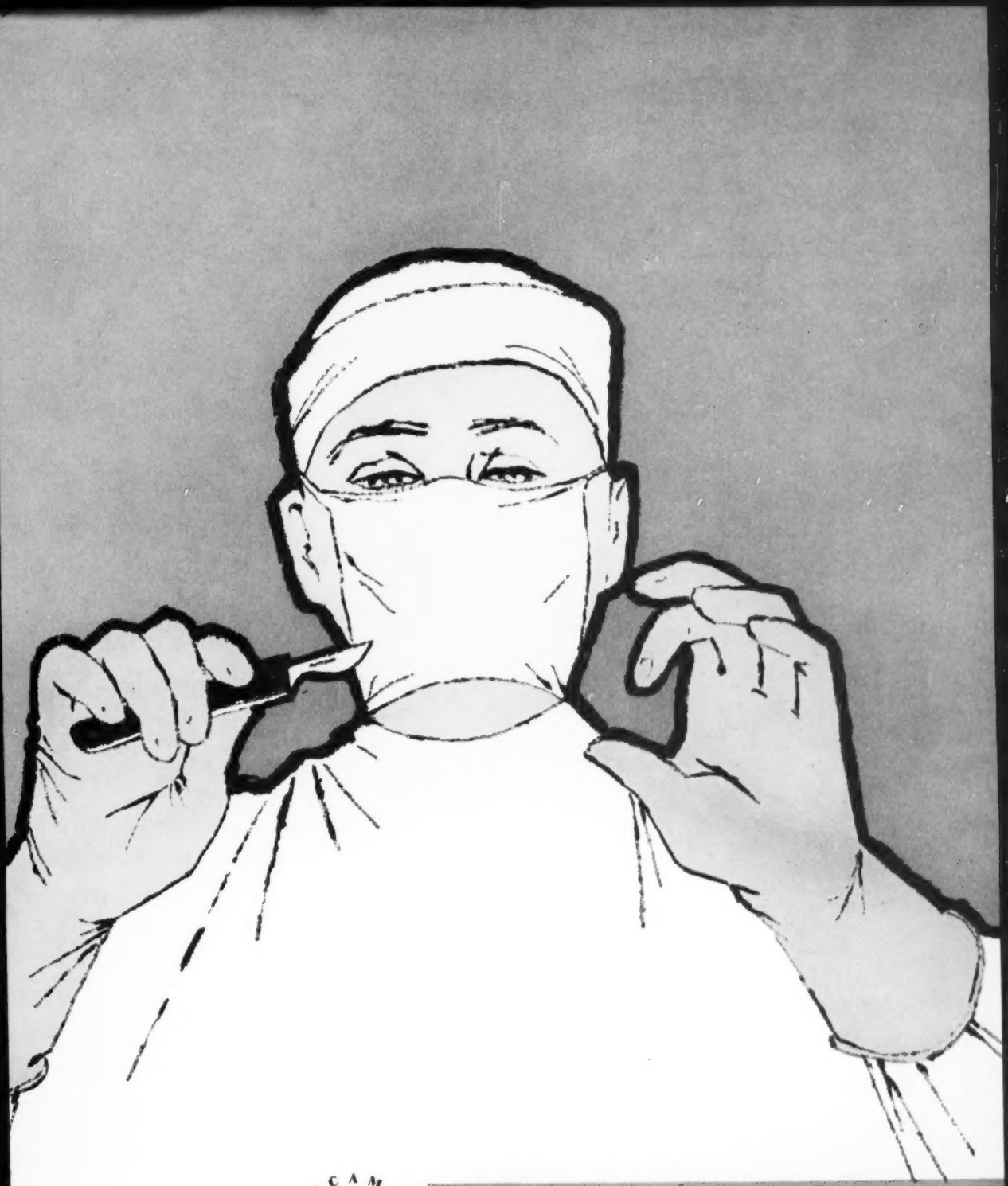

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